A Thesis in General Surgery

NEUTROPHILIC LYMPHOCYTIC RATIO AS A PROGNOSTIC INDICATOR IN ACUTE PANCREATITIS

Submitted in partial fulfillment of the
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APRIL – 2014

DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation titled "**NEUTROPHILIC LYMPHOCYTIC RATIO AS A PROGNOSTIC INDICATOR IN ACUTE PANCREATITIS"** is a bonafide and genuine research work carried out by me under the guidance of Dr.R.A.Pandyaraj M.S., Professor, Department of General Surgery, Kilpauk Medical College, Chennai.

This dissertation is submitted to THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY, CHENNAI in partial fulfillment of the requirements for the degree of M.S. General Surgery examination to be held in April 2014.

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ABSTRACT

Background:

Acute pancreatitis is a common and a highly challenging clinical condition encountered in our day to day surgical practice. Severe pancreatitis being associated with high mortality, scoring systems has been devised to assess the severity. The Neutrophil-Lymphocyte Ratio (NLR) calculated from the WBC differential count provides a rapid indication of the extent of an inflammatory process.

Aim of study:

To investigate if Neutrophil- Lmphocyte Ratio (NLR) can act as a single indicator in assessing the prognosis of acute pancreatitis.

Materials & methods:

The NLR was calculated on 100 acute pancreatitis patients on day 0, day1 and day2 of admission. The NLR obtained was correlated with the severity of pancreatitis using Atlanta classification.

Results:

Of the 100 patients, 20 patients had severe acute pancreatitis. The NLR values calculated in severe acute pancreatitis was significantly higher than in mild acute pancreatitis on all 3 days (Day 0- 8.2 vs. 4.4; Day 1- 9.07 vs. 5.08; Day 2- 10.89 vs. 4.52).

Conclusion:

Elevation of Neutrophil Lymphocyte Ratio (NLR) during the first 48hrs of admission is significantly associated with severe acute pancreatitis and can be used as a simple, single, cost-effective indicator in assessing severity of acute pancreatitis.

Key words: Acute Pancreatitis, Neutrophil Lymphocyte Ratio (NLR), Severity

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INTRODUCTION

Acute pancreatitis (AP) is an outcome of acute inflammation of pancreas with activation of the pancreatic enzymes. The Atlanta classifies acute pancreatitis into mild pancreatitis and severe pancreatitis. Though normally it is a self limiting process with 80 % having mild disease, 10% to 20% of them have a rapidly progressive inflammatory response. Patients with mild pancreatitis have less than 1% mortality rate whereas even up to 50% for those with severe pancreatitis.

In Severe pancreatitis, adverse outcome is attributed to an uncontrolled systemic inflammatory response syndrome (SIRS), with progression to a multi-organ dysfunction syndrome (MODS). Hence to stratify the severity of the Acute Pancreatitis, Scoring Systems have been introduced which help in appropriate management and to improve the outcome.

The scoring system currently regarded as the best for assessment of Acute Pancreatitis, namely the Acute Physiology and Chronic Health Evaluation (APACHE II), is labor intensive and is not being followed routinely for patients of pancreatitis treated outside Intensive Care Unit. Other scoring systems namely Ransons scoring system and Imrie scoring

system (Glascow scoring system) are also difficult to apply as there are many parameters.

In India, pancreatitis seems to be more common among alcoholics. Being a developing nation, most of the affected families live in poverty. So, the hospital expenses in treatment of pancreatitis are a burden to them. Many investigations are required for calculating the above severity scoring systems which will increase the patient's cost. In order to predict the severity of the disease earlier, a simple scoring system is needed which will enable us to provide aggressive treatment for those progressing to severe pancreatitis and lower the morbidity and mortality.

The white blood cell count is a routine serum hematological test that is already incorporated in many of the current Acute Pancreatitis scoring systems, and routinely performed on all surgical emergency admissions. Components of the total WBC count include neutrophils and lymphocytes, both of which can be used individually as markers of inflammation.

In Acute pancreatitis, Neutrophils are incorporated into the pancreas due to the action of inflammatory cytokines. These neutrophils propagate Systemic Inflammatory Response Syndrome (SIRS) and the inflammatory cascade in Acute Pancreatitis whereas lymphocyte depletion occurs in severe

sepsis, and is associated with a poor outcome. This lymphopenia has been previously associated with severe sepsis, bacteremia, and surgical stress.

The Neutrophil-Lymphocyte ratio (NLR) is a measure of the divergence of these two WBC components, and may be more accurate than the total WBC or individual neutrophil and lymphocyte counts in predicting poor outcome.

Thus the aim of my study is to check if NLR can be used as a single cost-effective tool to predict the severity of acute pancreatitis.

AIMS AND OBJECTIVES

The aim of my study is to calculate the Neutrophilic Lymphocytic Ratio (NLR) among acute pancreatitis patients and to investigate if this ratio is helpful as a single predictor in assessing the prognosis of acute pancreatitis.

REVIEW OF LITERATURE

HISTORICAL BACKGROUND:

The pancreas is a hidden organ and was one of the last organs in the abdomen to be analyzed by anatomists, physiologists, physicians, and surgeons.[1] Earliest reference dates back to the Babylonian *Talmud* which describes pancreas as the "finger of liver". The word pancreas is derived from a Greek concept of *pan kreas* (meaning "all flesh") based on the hypothesis by Hippocrates that all glandular structures were composed of flesh.[2]

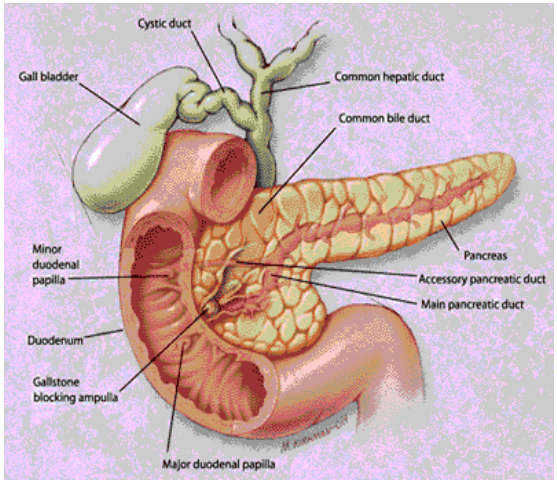
Vesalius was the first initiated the formal structural elucidation of pancreas. The formal structure of pancreas was first quoted by Vesalius. The physiologic function of pancreas was defined by R. de Graaf. The association of diabetes mellitus with pancreas was identified by O. Minkowski. With regard to the digestive property of pancreas, fat digestion was described by J. Purkinje and role of trypsin in proteolysis by W. Kuhne.[2]

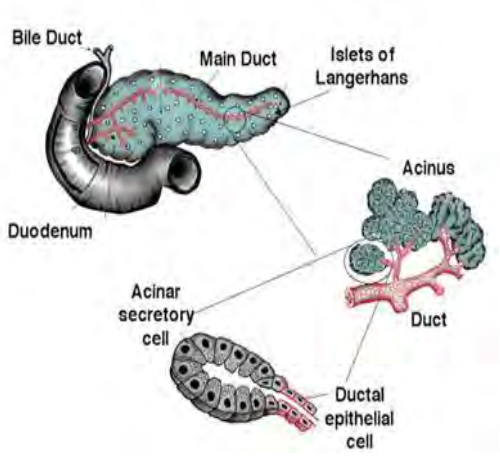
Nicholaes Tulp from Amsterdam was the first to describe acute pancreatitis in 1652. However, Guy Patin from Paris made a similar observation, but published a decade later.[2]

PANCREAS:

The pancreas is a retroperitoneal organ which has both exocrine and endocrine functions. In man, it is divided into different parts like head, body, and tail, with the head of pancreas enclosed by the duodenum and the tail which abuts the spleen. The pancreatic cells are characterized into three distinct types of cells, namely the acinar cells, endocrine cells and the ductal cells. The acinar cells group to form acini which in turn form distinct lobules and secrete the digestive enzymes. The ductal cells form the pancreatic duct which joins with the common bile duct and opens into the second part of duodenum. The endocrine cells namely the Islets of Langerhans secrete hormones which help in regulation of glucose uptake, release and maintenance of serum glucose levels.[3, 4, 5]

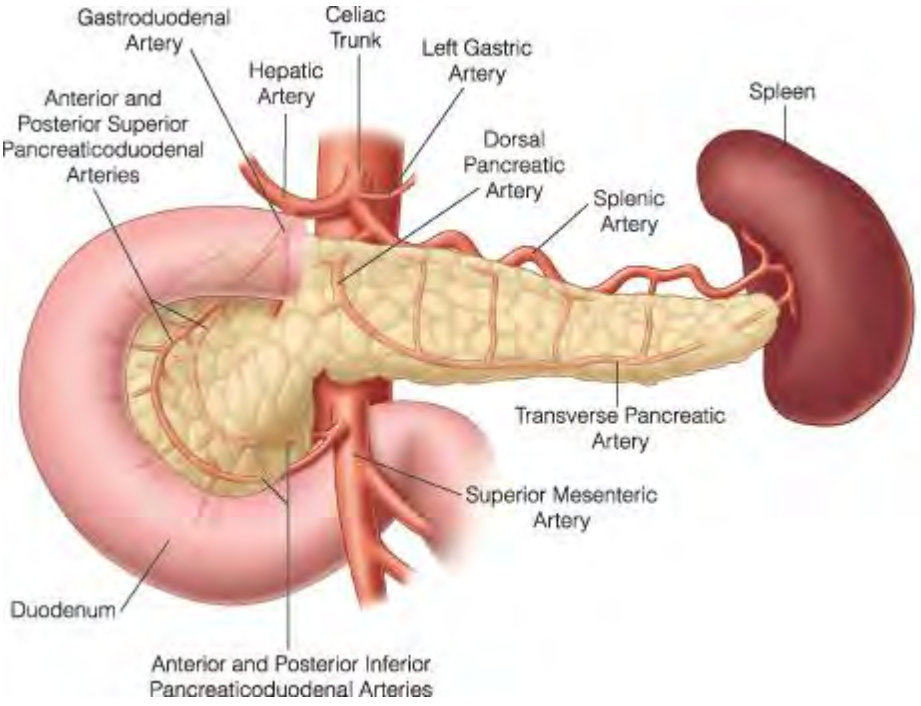
Fig 1: Anatomy of Pancreatic cells and the Ductal system





The blood supply of pancreas is derived from the Superior and Inferior Pancreaticoduodenal arteries and branches from the Splenic artery. Venous drainage is by Splenic vein, Superior mesenteric vein and the Portal veins. Lymphatics drain into the Splenic, Celiac and Superior mesenteric lymph nodes.

Fig 2: Blood Supply of Pancreas



Pancreas plays an important role in digestion and absorption of food from the gut. It also regulates glucose homeostasis. Humoral control is by two hormones namely secretin and pancreozymin secreted by duodenum and

proximal jejunum. Secretin induces alkaline secretion and pancreozymin produces juice rich in amylase, lipase, and trypsinogen.

ACUTE PANCREATITIS:

Acute pancreatitis is a common clinical condition encountered in our day to day surgical practice. Even though the volume of cases is high, acute pancreatitis poses a great challenge to the treating surgeon.

In 1925, Lord Moynihan stated that, in connection with the abdominal viscera, the dreaded calamity is the Acute Pancreatitis. He substantiated his statement with the following features of acute pancreatitis „Its sudden onset, unbearable agony and the mortality rate depending on its severity are the aspects of acute pancreatitis, which make it the most formidable to overcome'.[6]

Acute pancreatitis is an inflammation of the pancreatic tissue secondary to acinar cell necrosis. It occurs due to auto digestion by pancreatic enzymes.

Epidemiology:

As per data from the US, UK and Denmark, the incidence of acute pancreatitis varies between 4.8 to 24.2 cases per 100,000 population[7] .Yet no prevalence data are available in India.

Most patients develop a mild and a self-limited course, however 10% -20% of patients have a rapidly progressive course with prolonged length of hospital stay and significant morbidity and mortality. Mild pancreatitis is associated with a mortality rate of less than 1% but, it increases up to 10%-30% in severe pancreatitis.[8]

CLASSIFICATION:

In 1992, the International Symposium in Atlanta was conducted on acute pancreatitis. According to it, acute pancreatitis was classified into mild and severe pancreatitis. Severe pancreatitis is diagnosed if there is any evidence of organ failure or local pancreatic complications.[9]

Table 1: Atlanta classification of Acute Pancreatitis

Classification	Clinical features	Morphologic findings
Mild ("edematous pancreatitis")	Minimal organ dysfunction and uneventful recovery	Interstitial edema and disseminated, usually microscopic, fatty tissue necrosis

Severe (“necrotizing pancreatitis”)	Organ failure and/or local complications such as necrosis, abscess, or pseudo cyst	Extensive fatty tissue necrosis and/or hemorrhagic necrosis involving both the pancreatic parenchyma and the extra pancreatic fatty tissue: development of pseudo cysts and abscesses

Definition of organ failure by Atlanta
• Shock–systolic pressure <90 mmHg • PaO2 ≤60 mmHg • Creatinine >2.0 mg/L after rehydration • Gastrointestinal bleeding >500 cc/24 h

OTHER DEFINITIONS:

- **Pancreatic necrosis:**

It is the non viable pancreatic tissue which can be focal or diffuse and is usually associated with peripancreatic fat necrosis. It can be infected or sterile.

- **Acute fluid collection:**

It is the fluid found inside or around the pancreas which does not have a definitive wall. It usually occurs in the earlier stages of acute pancreatitis in around 30% - 50% patients and resolves spontaneously.

- **Pancreatic pseudocyst:**

It is the fluid collection that remains for 4 - 6 weeks and is walled off by fibrous or granulation tissue.

- **Hemorrhagic pancreatitis:**

It is pancreatitis associated with hemoperitoneum which occurs due to erosion of pseudoaneurysm of the peripancreatic blood vessels. It can sometimes erode the retroperitoneal vessels resulting in acute hemorrhage which is an acute emergency. Management for this hemorrhage requires immediate angiographic embolisation or surgery.

PATHOPHYSIOLOGY:

Acute pancreatitis is a final result of abnormal pancreatic enzyme activation inside acinar cells. Trypsin which is derived from trypsinogen is the principal activator of all enzymes. Even normally a small proportion of trypsinogen gets activated spontaneously inside the acinar cells. But the various protective mechanisms present within pancreas wash out the activated trypsin so that there won't be any damage to the gland.

These include:

- Serine Protease Inhibitor Kazal type 1 (SPINK1)
- Mesotrypsin
- Enzyme Y
- α1-antitrypsin
- α2-macroglobulin

In acute pancreatitis, Colocalisation is the first step as per Immunolocalisation studies. After a pancreatic injury, the above defensive mechanisms are overcome, zymogen granules and lysosome granules containing enzymes like cathepsin B colocalise inside the acinar cells resulting in intra acinar pancreatic enzyme activation.[8]

This induces auto digestion of the pancreatic parenchyma. In response, the acinar cells release pro-inflammatory cytokines such as TNF-α

(Tumour Necrosis Factor-α), IL-2, IL-1 and IL-6 .These mediators propagate the response both locally and systemically.

Neutrophils and macrophages are recruited in to the pancreatic parenchyma which cause the release of more TNF-α, IL-1, IL-6, reactive oxygen species, prostaglandins, platelet activating factor and leukotrienes. This further increases the permeability and damages the microcirculation of the pancreas.[8]

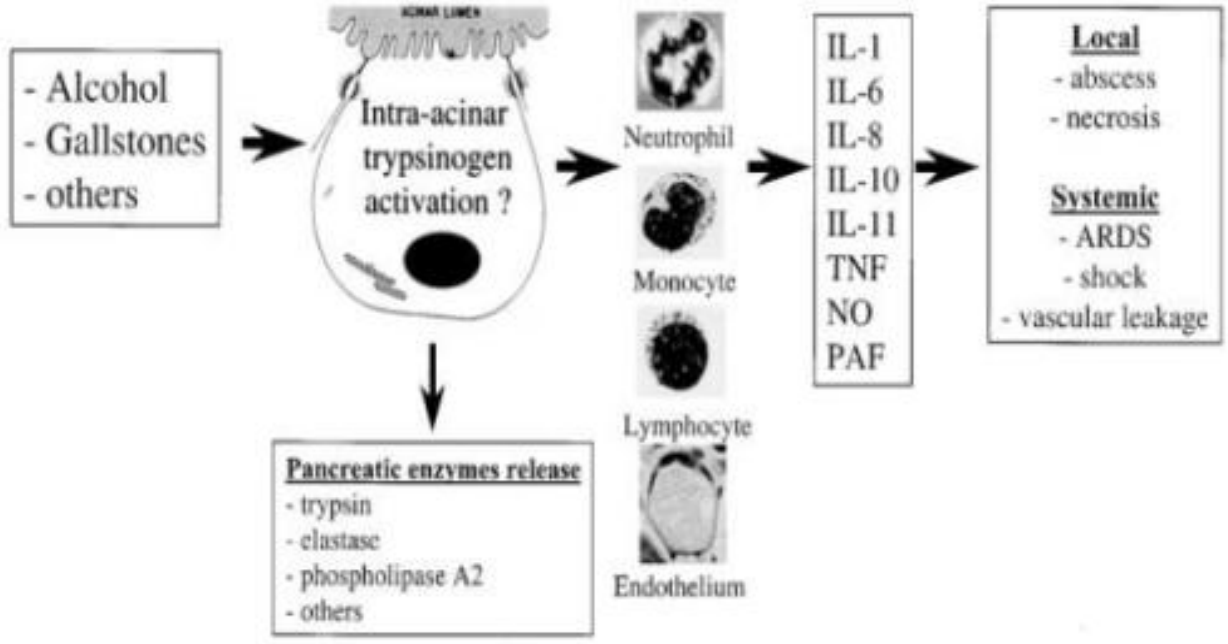


Fig 3: Pathophysiology of Acute Pancreatitis

The inflammatory cascade is self-limited in approximately 80% - 90% of patients. In small number of patients, there is massive release of inflammatory mediators into systemic circulation. Active neutrophils mediate acute lung injury and induce adult respiratory distress syndrome

(ARDS). Similarly it affects the kidneys and gut and progresses to Multi-Organ Dysfunction Syndrome (MODS).

Also Trypsin activates other pathways, such as complement, coagulation or fibrinolysis, extending the process outside the gland which is responsible for systemic manifestation of the disease.

Genetic factors have also been implicated in pathogenesis of acute pancreatitis which is:

- Cationic Trypsinogen gene (PRSS1)
- Cystic Fibrosis Transmembrane Conductance Regulator Gene (CFTR)
- Polymorphisms in SPINK1

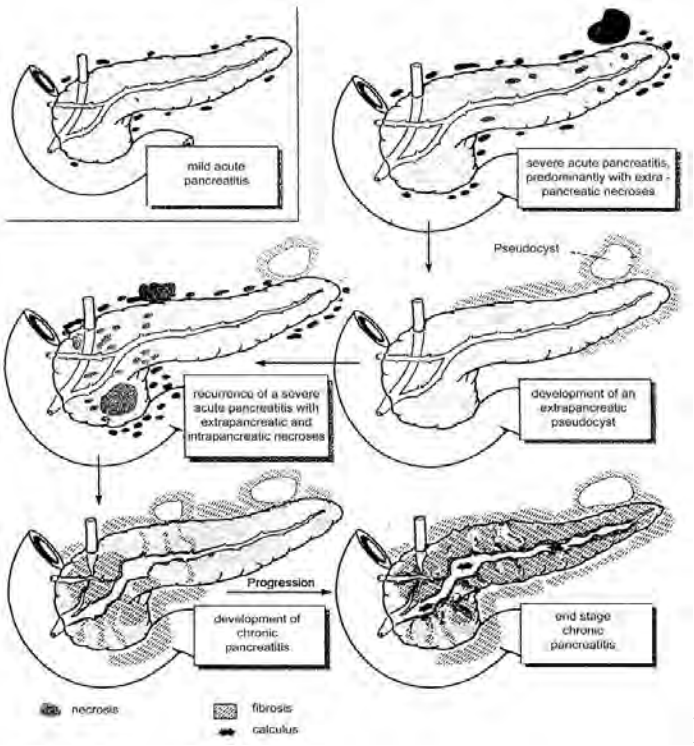


Fig 4: Events of Acute Pancreatitis

ETIOLOGY:

Gall stones and Alcohol are the most common (70% to 80%) causes of pancreatitis.[8] Other etiological factors are as follows:

Table 2: Etiological factors of Pancreatitis

Other causes
Shock
Toxins • Scorpion venom, • Methyl alcohol, • Organophosphorous insecticides
Drugs • Alpha- methyldopa • 5-Aminosalicylate (mesalamine) • Azathioprine • Furosemide • Isoniazid • 6- Mercaptopurine • Metronidazole • Dexamethasone • Trimethoprim/sulfamethoxazole

• Antiretroviral drugs
Metabolic- hypertriglyceridemia, Hypercalcemia
Ductal obstruction- • Tumors, • Parasites, • Duodenal diverticula, • Annular pancreas, • Choledochocele
Surgical procedure- ERCP
Trauma
Infection • Viral- Mumps, Coxsackie A, HIV, CMV • Bacterial- M.tuberculosis • Mycoplasma Hereditary/ familial/ genetic

Biliary Pancreatitis:

It is one of the commonest etiologies of acute pancreatitis. Studies have shown that, episodes of acute pancreatitis are frequently preceded by

passage of stone into the duodenum. In about 90% of patients with stone induced pancreatitis, stones can be retrieved from their stools.

Various mechanisms have been proposed for biliary pancreatitis.

- The theory proposed by Opie, termed as "Common channel theory". The lodging of biliary stone in the common channel between the biliary tract and the pancreatic duct causes pancreatitis as a result of reflux of bile into the pancreatic duct.

- Numerous studies have shown that the above theory may be not being as appropriate as the bile reflux is not sufficient to cause acute pancreatitis. This paves the way for the proposal of "Duct obstruction theory", which states that the edema induced by the stones leads to the obstruction of the duct which in turn results in duct hypertension, triggering pancreatitis.[8]

Alcohol Induced Pancreatitis:[8]

Although alcohol is the most frequent cause for chronic pancreatitis, it can also cause acute episodes. Various mechanisms have been proposed for pancreatitis induced by alcohol.

- Ductal hypertension caused by alcohol induced spasm of sphincter of oddi.

- Free fatty acids produced by alcohol induced hypertriglyceridemia have a toxic effect on the pancreatic acinar cells.
- Alcohol stimulates the production of free radicals within the pancreas which in turn injure the acinar cells.
- Pancreatic ischaemia caused by alcohol induced microcirculation failure.
- Alcohol stimulates the pancreatic acinar cells to produce protein-rich pancreatic juice, which has the following effects,

    -Formation of protein plug by the protein rich fluid, which causes duct obstruction.

    -The protective enzymes are overwhelmed resulting in auto-digestion of pancreas.

Idiopathic Pancreatitis:

In spite of extensive studies, in about 20% of patients presenting with acute pancreatitis, no cause can be identified.

The mechanisms proposed in such instances are:

- Sludge or microcrystals in the gall bladder
- Dysfunction of the sphincter leading to ductal hypertension

- Subclinical mutations in cystic fibrosis transmembrane regulator gene (CFTR gene)

CLINICAL FEATURES:[8]

Symptoms:

- Abdominal pain is the most common symptom. the pain is usually
  - Epigastric radiating to the back
  - Constant severe pain
  - Typically relieved by leaning forward
- Nausea and vomiting
- Dyspnoea if there is associated pleural effusion

Signs:

- General examination reveals dehydration, tachycardia, tachypnoea, hypotension
- Abdominal examination usually reveals severe epigastric tenderness associated with guarding and rigidity
- Bowel sounds may be absent due to paralytic ileus
- Retroperitoneal hemorrhage leading to bluish discoloration in
  - Umbilical area- Cullen's sign
  - Loin- Grey Turner's sign

- Groin- Fox’s sign

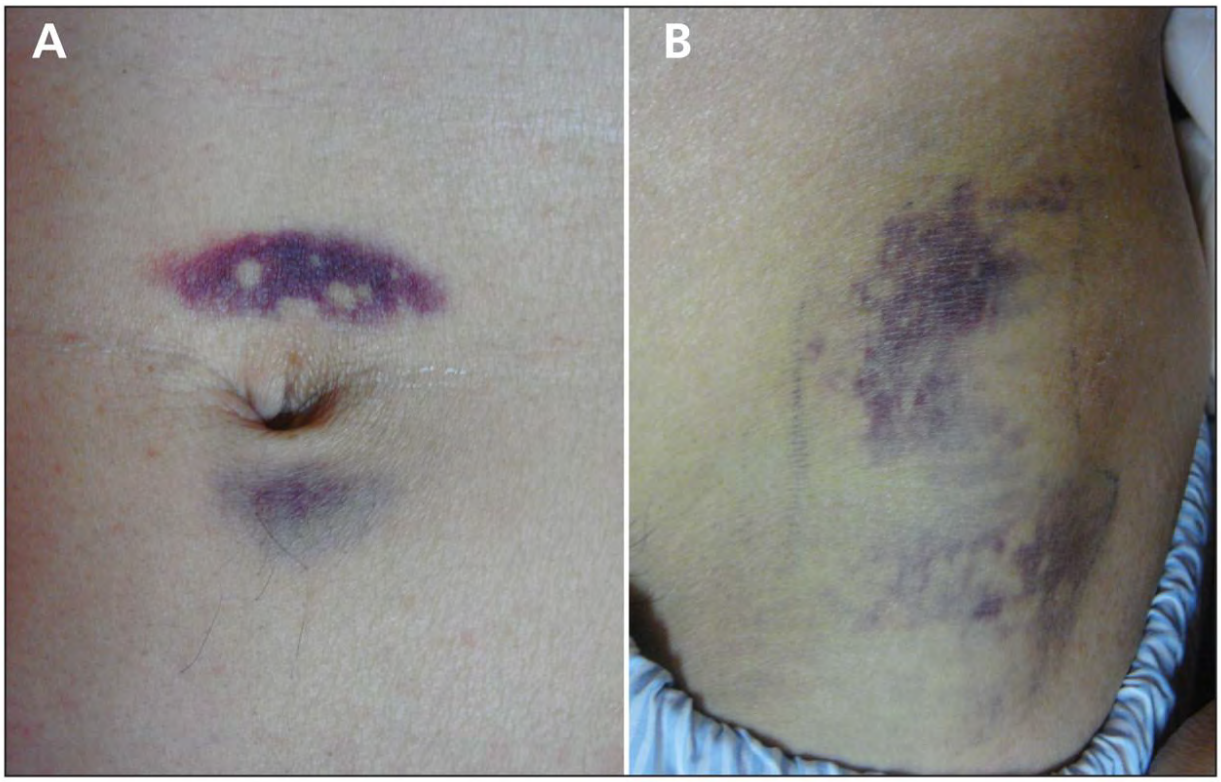


Fig 5: A) Cullens sign B) Grey Turner’s sign

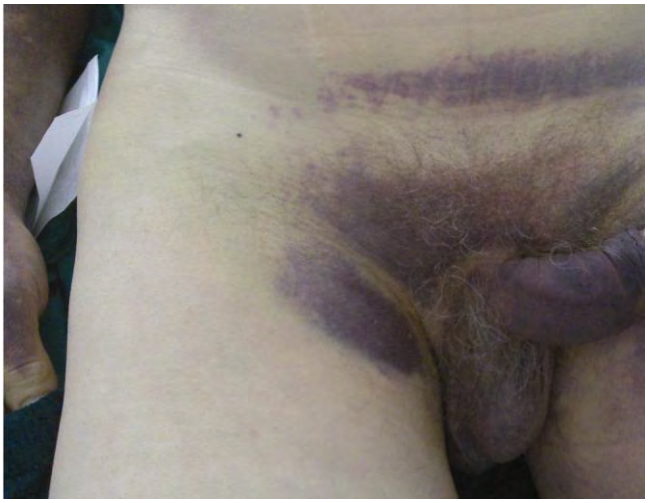


Fig 6: Fox’s sign

- Pain or resistance in the zone where the head of pancreas is located (in the epigastrium, 6–7 cm above the umbilicus) - Korte's sign

- Pain with pressure under the xiphoid process - Kamenchik's sign
- Tenderness on pressure at the Mayo-Robson's point - a point at the junction of the inner 2/3 and the outer 1/3 of the line that represents the bisection of the left upper abdominal quadrant. At this point the tail of pancreas is projected on the abdominal wall.
- Thrombophlebitis in the legs

INVESTIGATIONS:

A. Blood investigations:

➢ *Serum Amylase:* Most common serum marker used in diagnosis. It elevates within 2-12 hours of onset of symptoms and remains elevated for 3-6 days. In acute pancreatitis there is loss of cell to cell adhesions and so amylase gets access to vessels and is increased in serum. It has no prognostic value.

Extrapancreatic sources of amylase need to be considered which are the salivary gland, lung, ovary, prostate. Other causes of hyperamylasemia also need to be considered like acute cholecystitis, intestinal ischaemia, hollow viscus perforation, intestinal obstruction and macroamylasemia.

- *Serum Lipase:* More specific for pancreas. Its limitation is that it remains elevated for 1 week, so it is not sensitive enough to detect complications.
- *Other investigations:*
    i. Increased hemoglobin, hematocrit, Blood Urea Nitrogen (BUN) and creatinine due to hypovolemia.
    ii. Hypoalbumunemia secondary to fluid replacement with crystalloids
    iii. Hyperbilirubinemia which may be a cause or effect of acute pancreatitis
    iv. Hypocholeremic metabolic alkalosis secondary to excessive vomiting
    v. Hypocalcemia due to sequestration in pancreatic fat necrosis or associated hypoalbuminemia
    vi. Hyperglycemia due to associated diabetes mellitus, increased glucagon release, increased catecholamine release.

B. Imaging Studies:

- *X-Ray Abdomen:* Not specific for pancreatitis, but may show signs due to ileus
    1. Sentinel loop sign

2. Colon cut-off sign

3. Renal halo sign

- *Ultrasonography abdomen:* limited value in visualizing pancreas since it is usually obscured by bowel gas shadows. However, when detected following findings may be noted

1. Bulky edematous pancreas

2. Any associated biliary stone

3. Dilated pancreatic duct

4. Any fluid collections

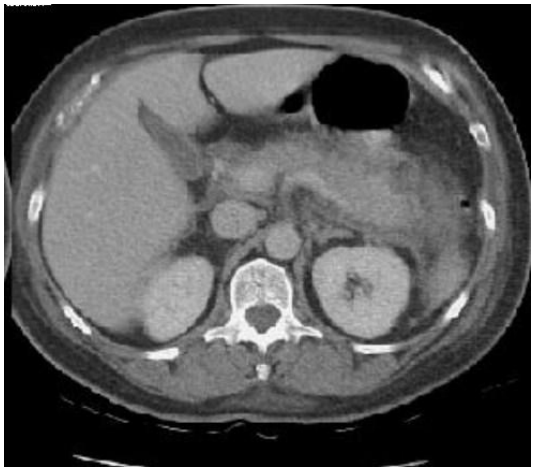


Fig 7: USG abdomen showing bulky hypo echoic pancreas

Fig 8: CT showing features of Acute pancreatitis

- *CECT Abdomen:* it is the investigation of choice to diagnose acute pancreatitis and its complications. Following features may be noted

1. Enlarged pancreas

2. Loss of peri pancreatic fat plane
3. Areas of deceased density
4. Localized fluid collection
5. Detects pancreatic necrosis which is of great importance which is identified by non enhancement of > 30% or > 3cm of parenchyma of pancreas.

CT is usually performed around 48hours after diagnosis as earlier done CT misses necrosis. The sensitivity of CECT to detect necrosis at 4 days is 100%.[10]

- *MRI Abdomen:* Can also be used in diagnosis and staging severity. Usually taken when CECT is contraindicated like in case of renal dysfunction or contrast allergy. Following table compares various imaging modalities used in acute pancreatitis[10]:

Table 3: Comparison of various imaging modalities in acute pancreatitis

Imaging Technique	Effectiveness
CECT abdomen	78 % sensitivity and 86% specificity for severe acute pancreatitis
Endoscopic USG	100 % sensitivity and 91 % specificity for gallstones

MRCP	81 to 100 % sensitivity for detecting CBD stones
	98 % negative predictive value and 94% positive predictive value for bile duct stones
	As accurate as CECT in predicting severity of pancreatitis and identifying pancreatic necrosis.
MRI	83% sensitivity and 91% specificity for severe acute pancreatitis
USG abdomen	87 to 98% sensitivity for the detection of gallstones.

DIAGNOSIS:

Diagnosing acute pancreatitis requires clinical, serological and imaging correlation. Various serum markers are used in the diagnosis and prognosis of acute pancreatitis. Some of them have been summarized in the following table.[11]

Table 4: Various Serum markers in Acute Pancreatitis

Laboratory Test	Time of onset (Hours)	Purpose	Clinical observation / limitations
Alanine transaminase	12 to 24	Diagnosis and etiology	Associated with gallstone pancreatitis; threefold elevation or greater in the presence of acute pancreatitis has a positive predictive value of 95 percent in diagnosing acute gallstone pancreatitis
Amylase	2 to 12	Diagnosis	Most accurate when at least twice the upper limit of normal; amylase levels and sensitivity decrease with time from onset of symptoms
C-reactive protein	24 to 48	Predictive of severity	Late marker; high levels associated with pancreatic necrosis
Interleukin-6	18 to 48	Predictive of severity	Early indication of severity
Interleukin-8	12 to 24	Predictive of severity	Early indication of severity

Lipase	4 to 8	Diagnosis	Increased sensitivity in alcohol-induced pancreatitis; more specific and sensitive than amylase for detecting acute pancreatitis
Phospholipase A2	24	Predictive of severity	Associated with development of pancreatic necrosis and pulmonary failure
Procalcitonin	24 to 36	Predictive of severity	Early detection of severity; high concentrations in infected necrosis
Trypsinogen activation peptide	Within few hours	Diagnosis and predictive of severity	Early marker for acute pancreatitis and close correlation to severity

The Atlanta symposium devised certain criteria for the diagnosis of acute pancreatitis. According to it, any two of the following three features is required for diagnosis: [9]

- Abdominal pain consistent with acute pancreatitis, i.e., severe and persistent epigastric pain, acute in onset, radiating to the back
- Serum amylase or lipase: three or more times the normal limit

- CECT (Contrast Enhanced Computerized Tomography) findings characteristic with acute pancreatitis and less commonly with MRI or Ultrasonography of abdomen

DIFFERENTIAL DIAGNOSIS:

- Biliary colic/ Acute cholecystitis
- Perforated hollow viscus
- Mesenteric ischaemia/ infarct
- Inferior wall myocardial infarction
- Closed loop intestinal obstruction
- Dissecting aortic aneurysm

COMPLICATIONS OF PANCREATITIS:

- ***Local:***
  - ✓ Fluid collections
  - ✓ Pancreatic Ascites/ Pleural effusion
  - ✓ Pseudocyst
  - ✓ Pancreatic necrosis
  - ✓ Pancreatic abscess
  - ✓ Pseudoaneurysm/hemorrhage
  - ✓ Splenic vein rupture

- ✓ Portal vein rupture
- ✓ Gastrointestinal bleeding
- ✓ Postnecrosectomy bleeding
- ✓ Splenic infarction
- ✓ Enteric fistula
- ✓ Smoldering pancreatitis:

In this entity, despite adequate supportive therapy, the pain persists for 2-3 weeks or more with persistent hyperamylasemia. The cause may be varied and includes any of the causes of acute pancreatitis. Imaging shows significant pancreatic injury suggesting a functional obstruction to the pancreatic duct secondary to edema or spasm. Transpapillary stenting relieves the symptoms.

- ❖ ***Regional:***
  - ✓ Venous thrombosis
  - ✓ Paralytic ileus
  - ✓ Intestinal obstruction
  - ✓ Intestinal ischaemia
  - ✓ Cholestasis

❖ ***Systemic:***

- ✓ SIRS
- ✓ MODS
- ✓ ARDS
- ✓ Renal failure
- ✓ Cardiovascular complications
- ✓ Hypocalcemia
- ✓ Hyperglycemia
- ✓ Disseminated Intravascular Coagulation
- ✓ Protein malnutrition
- ✓ Encephalopathy
- ✓ Fat necrosis (subcutaneous nodules)
- ✓ Retinopathy
- ✓ Death

SEVERITY SCORING SYSTEMS:

As there is high morbidity and mortality associated with severe acute pancreatitis, many scoring systems have been formulated to stratify the risk of developing severe pancreatitis. All the scoring systems have been devised keeping the Atlanta's classification as a standard. The Clinical scoring

system and certain laboratory tests are the most common methods of assessing the prognosis in acute pancreatitis.[12]The most commonly used systems are the Ranson's criteria, The Modified Glascow system (Imrie Scoring), APACHE II scoring system.

Ranson's criteria were devised in 1974 which consists of 11 parameters which are derived from patients at the time of admission and at 48 hours. Severe pancreatitis is defined if 3 or more of its parameters are fulfilled. The disadvantage of this criterion is that it can predict only at the end of 48 hours. Also it has a low positive predictive value (50%) but a high negative predictive value (90%).

Hence, it is mainly used to rule out a severe disease. The same is true for Imrie score.[8]

Table 5: Ranson's criteria (Non-Gallstone Pancreatitis)

At admission
☐ Age in years > 55 years
☐ Leucocyte count > 16000 cells/mm^3
☐ Blood glucose > 10 mmol/L (> 200 mg/dL)
☐ Serum AST > 250 IU/L
☐ Serum LDH > 350 IU/L

At 48 hours

☐ Calcium (serum calcium < 8.0 mg/dL)

☐ Hematocrit fall >10mmol/l

☐ Oxygen (hypoxemia PO2 < 60 mmHg)

☐ BUN increased by 5 or more mg/dL after IV fluid hydration

☐ Base deficit (negative base excess) > 4 mEq/L

☐ Sequestration of fluids > 6 L

Table 6: Ranson's criteria (Gallstone Pancreatitis)

At admission

☐ Age in years > 70 years

☐ Leucocyte count > 18000 cells/mm^3

☐ Blood glucose > 220 mg/dL)

☐ Serum AST > 250 U/100mL

☐ Serum LDH > 400 IU/L

At 48 hours

☐ Calcium (serum calcium < 8.0 mg/dL)

☐ Hematocrit fall >10mmol/l

☐BUN increased by 2 or more mg/dL after IV fluid hydration ☐ Base deficit (negative base excess) > 5 mEq/L ☐ Sequestration of fluids > 4 L

Interpretation: • Score < 3- Mild Pancreatitis • Score 4 to 6- Moderate Pancreatitis • Score > 7- Severe Pancreatitis

Table 7: Modified Glascow index (Imrie score)

The Glasgow criteria are valid for both gallstone and alcohol induced pancreatitis
• Age >55 years old • PaO2 < 8kPa • Neutrophilia – Leucocyte count >15x10(9)/L • Calcium < 2mmol/L • Urea > 16mmol/L •AST >200 IU/L; LDH > 600 IU/L • Serum Albumin < 3.2g/dl

• Blood glucose >180mg/dl
Interpretation: Scores 3 or more it indicates severe pancreatitis

The Acute Physiology and Chronic Health Examination (APACHE) II is one of the most widely used systems for early risk stratification in acute pancreatitis. It is based on patient's age, previous health status and 12 routine physiological parameters. An APACHE II score of 8 or more indicates severe disease. The main advantage of this system is that it can be used at the time of admission and at any time. However, its major drawback is that it needs multiple parameters and an online calculator for interpreting the severity.

There are modifications to this system which are:

- APACHE 3- here 5 additional criteria are included to increase the accuracy.[13]
- APACHE O- here clinical assessment of obesity is also included

Table 8: APACHE II Score

I. Physiologic variable ☐ Rectal temperature (ºC) ☐ Mean arterial pressure (MAP) in mm Hg ☐ Heart rate in beats/min ☐ Respiratory rate in breaths/min ☐ PaO2 in mm Hg ☐ Arterial pH ☐ Serum sodium in mEq/l ☐ Serum potassium in mEq/l ☐ Serum creatinine in mg/dl ☐ Hematocrit in percentage ☐WBC count/ mm^3 ☐ Glasgow Coma Score The total acute physiology score = sum of above points
II. Age Points Less than 44 years (0 point) 45-54 years (2 points)

55-64 years (3 points) 65-74 years (5 points) ≥75 years (6 points)
III. Chronic Health Points – points are assigned as below if the patient gives a history of severe organ insufficiency or is immunocompromised: For nonoperative or emergency postoperative patients (5Points) For elective postoperative patients (2 points)
The APACHE II score = I+II+III Interpretation: A score of > 8 is considered as severe pancreatitis

CT has become routinely used in the prediction and determination of disease severity. Balthazar and his associates established the CT severity index. However, using CT alone was associated with relatively high false-positive rates.

Table 9: CT Severity Index

Balthazar Grades
Grade A: Normal pancreas consistent with mild pancreatitis (0 points)
Grade B: Focal or diffuse enlargement of the gland without peripancreatic inflammation (1 point)
Grade C: Peripancreatic inflammation (2 points)
Grade D: Peripancreatic inflammation with single fluid collection (3 points)
Grade E: Peripancreatic inflammation with two or more peripancreatic fluid collections or gas in the pancreas or retro peritoneum (4 points)
Necrosis score:
Absence of necrosis (0 point)
Up to 33% necrosis (2 points)
33% to 50% necrosis (4 points)
>50% necrosis (6 points)
CTSI = Balthazar Grade Score + Necrosis Score
Interpretation:
0-3 points: Mild pancreatitis
4-6 points: Moderate pancreatitis
7-10 points: Severe pancreatitis

BISAP (Bedside Index for Severity in Acute Pancreatitis) score is a simple tool which comprises of 5 parameters. A score of more than 3 is associated with higher risk.

Table 10: BISAP score

• Blood urea nitrogen more than 25 mg/dL, • Mental status impairment, •SIRS (Systemic inflammatory response syndrome), defined as two or more of the following - Temperature < 36 or > 38° C - Respiratory rate > 20 breaths/min or $PaCO_2$ < 32 mmHg - Pulse rate > 90 beats/min - WBC counts < 4000 or > 12,000 cells/ mm^3 or > 10% immature bands • More than 60 years of age, and/or • Pleural effusion
Interpretation: A Score of more than 3 is associated with 7 to 12 fold increase in risk of organ failure.

Other biochemical markers include as follows:

- C - reactive protein (CRP):

CRP is an acute-phase reactant produced by the liver and is used extensively as a marker of severe pancreatitis. However it is non specific as its levels rise in most inflammatory conditions. The limitation with CRP is that it can be measured only after 48hrs as it lacks sensitivity before 48hrs.

- Polymorphonuclear Leukocyte Elastase:

Polymorphonuclear leukocyte elastase rises very early, even before CRP, in acute pancreatitis. High levels have been reported to differentiate severe from mild disease.

- Phospholipase A2 (PLA2):

PLA2 is involved in the release of prostaglandins from cell membranes and degrades surfactant in the lung. It plays a role in the pulmonary dysfunction associated with acute pancreatitis. Levels of catalytic type II PLA2 are used to differentiate between mild and severe disease within 24 hours of admission

- Urinary Trypsinogen Activation Peptide (TAP):

Urinary TAP may serve as an early predictor of severity in patients with acute pancreatitis. Elevated urinary TAP >30 nmol/L correlates with disease severity. The test can be applied within 12 hours of admission. The positive predictive value of an elevated TAP is 80% and the negative predictive value approaches 100%.

- Procalcitonin:

This propeptide is another acute-phase reactant that has been shown to differentiate mild from severe acute pancreatitis within the first 24 hours after symptom onset. A serum strip test that has a sensitivity of 86% and a specificity of 95% in detecting organ failure has been developed. It has a drawback that it is not available at all centres and is expensive.

- Interleukin-6 (IL-6):

IL-6 is an acute-phase reactant cytokine that is produced by a variety of cells and induces hepatic synthesis of CRP. Several studies have shown that it is a reasonably good marker to differentiate mild from severe disease, but the test is not readily available in all centres and is very expensive.

- Serum Amyloid A:

Serum amyloid A is another early acute-phase reactant that is synthesized in the liver and is associated with the extent of tissue inflammation. Studies have demonstrated that the level of this serum protein can differentiate mild from severe disease. However, it is expensive and not available in peripheral centres.

It can be noticed that the limitation with other parameters is that they are very costly and not easily available.

- LDH (Lactate dehydrogenase) **:**

Chen and coworkers 63 found that in 42 patients with acute pancreatitis, serum LDH activity was significantly higher in severe than in mild attacks. Moreover, by evaluating the distribution of the five known LDH isoenzymes, they found that LDH-4 and LDH-5 were the only isoenzymes increased during the disease and that LDH-4 was the only isoform that could differentiate between severe and mild attacks. However, because the predominant pancreatic isoenzymes are LDH-2 and LDH-3, these results showed that the pancreas was not the major source of LDH.

Lactate dehydrogenase (LDH) has been reported to be a sensitive indicator of pancreatic necrosis. In patients with biliary

pancreatitis, however, liver enzymes are generally elevated early in the course of the disease because of acute inflammatory liver cell injury caused by ampullary stones impacted during their transpapillary passage.

Accordingly, the identification of pancreatic necrosis using the initial high LDH activity as an indicator of necrosis may not be accurate.

In a study by Isogai and co workers it was proved that an elevation of the ratio of LDH to aspartate aminotransferase (AST) (LDH/AST) would better reflect pancreatic necrosis in biliary pancreatitis.

On realizing the importance of acute pancreatitis, extensive studies were conducted by numerous medical practitioners regarding evaluation of the severity of acute pancreatitis and designed various scoring systems. They also even compared these scoring systems with one another to find out a single best possible way to predict the severity of acute pancreatitis. The following are few examples of such studies.

In 2012 (April), Thomas L Bollen et al compared the radiological and clinical scoring systems in acute pancreatitis in his study and came to a

conclusion that routine CT abdomen, on admission is not recommended in a case of acute pancreatitis for assessing its severity.[14]

In 2012 (March), Rawad Mounzer et al, in his study, compared all clinical scoring systems which are currently in use to predict organ failure, which is one of the grave catastrophes of acute pancreatitis. He finally came to a conclusion that all scoring systems have reasonable accuracy in predicting persistent organ failure, but the Glascow score was found to be the best.[15]

In 2012 (Feb), Fabre et al compared several scoring systems in paediatric age group presenting with acute pancreatitis. He studied the sensitivity and specificity of each score and compared with one another and he found that the best parameter to assess the severity of acute pancreatitis in paediatric population is CT severity score.[16]

In 2011 (September), Zhang WW et al, on comparing the clinical scoring and CT severity scoring, he found that CT has superior role than clinical scoring in depicting the extra-pancreatic inflammation spread in cases of acute pancreatitis and he also found that CT severity index has good correlation with APACHE II and Ranson's scores.[17]

In 2011 (May), Su Mi Woo et al did an extensive study about serum Procalcitonin in predicting the severity of acute pancreatitis and he

compared the same with other severity indices. He inferred that, serum Procalcitonin was a simple promising biomarker as its accuracy in predicting the severity of acute pancreatitis, is similar to other scoring systems such as APACHE II score.[18]

In 2011 (Jan), Chavarri Herbozo et al conducted a study about hemoconcentration as an early predictor of severity in acute pancreatitis and compared it with other scores such as APACHE II and Ranson's scores. He found that hemoconcentration as a single parameter, is not much useful in predicting the severity in patients with acute pancreatitis.[19]

In 2007, Ekrem et al conducted a study and found out definite relation between the elevation of the following parameters and mortality and morbidity in patients presenting with acute pancreatitis. The parameters include CRP, BUN, LDH, CT severity index and APACHE score.[20]

In 2006, Yuk Pang et al, in his study compared Ranson's score with APACHE scores in 101 patients of acute pancreatitis and concluded that APACHE II score is more accurate than that of Ranson's score in predicting the severity of acute pancreatitis.[21]

In 2005, Ting-Kai Leung et al conducted a study which spanned over five years. In his study, he compared Ranson's and APACHE II scores with that of helical CT in predicting the severity of acute pancreatitis and he

found that the former is inferior to Balthazar computed tomography severity index in predicting acute pancreatitis outcome.[22]

The WBC count is a well known marker of infection and inflammation, and is part of many scoring systems in acute pancreatitis including Ranson, Imrie and APACHE II. The total WBC count comprises of neutrophils and lymphocytes both of which are individually markers of inflammation. It has been identified that following an insult, there is neutrophilia and lymphocytopenia which occurs within 4 to 8 hours as a response to severe infection, surgical stress, systemic inflammation and septic shock.

As per Mahidhara and Billiar, the reason for neutrophilia is due to delay in apoptosis of neutrophils, demargination of neutrophils from endothelium and as an effect of growth factors.

Hotchkiss et al, Ayala et al and many others have observed apoptosis of lymphocytes which resulted in lymphocytopenia. Menges et al supported this with his flow cytometric assays which showed a decrease in T4- helper lymphocytes following multiple trauma and hence responsible for SIRS and MODS. It has been stated that lymphocytopenia not only indicates the severity of the stressful condition, but also reflects the efficacy and adaptability of the immune system.

The response of the inflammatory/ immune system to stress can be easily assessed by the ratio of neutrophil count (in %) to lymphocyte count (in %). As per a study by Zahorec et al the severity of insult, severity of clinical status and clinical outcome, was found to correlate nicely with neutrophil/lymphocyte ratio with regard to APACHE II and SOFA scoring systems. He has suggested that when the differential counts of WBC were serially monitored, it provided information about the body's immunological response to stress in critically ill patients.[23]

In Acute pancreatitis, neutrophils propagate inflammation and tissue destruction via activation of a cascade of inflammatory cytokines (IL-6, IL-8, and TNF-α), proteolytic enzymes (myeloperoxidase, elastase, collagenase, and β - glucoronidase), and oxygen free radicals. An increase in neutrophil numbers corresponds with the development of SIRS and progression to MODS, which are hallmarks of Severe Acute pancreatitis. This Uncontrolled inflammation is thought to precipitate lymphopenia by lymphocyte redistribution and accelerated apoptosis, and lymphopenia.[24]

It is the divergence of these two components of the WBC counts namely neutrophilia and lymphopenia that led to the proposal of assessing the NLR as a single and more accurate predictive factor than either component alone. This has been assessed by Suppiah A et al, Azab et al and

Vedat Goral et al and they have uniformly accepted that the NLR is a simple indicator of severity in patients presenting with acute pancreatitis.[24, 33, 34]

TREATMENT:[8]

Treatment of acute pancreatitis depends on the severity of pancreatitis. Most of the cases of pancreatitis are managed conservatively except in cases of acute severe necrotizing pancreatitis and complications which warrants surgical intervention.

Aggressive fluid resuscitation, control of pain, strict monitoring of hemodynamic status, nutritional support, and surveillance for complications are important in management of patients with acute pancreatitis.

The cornerstone of the treatment of pancreatitis is aggressive volume repletion using crystalloid solution. The rate of administration should be individualized and adjusted based on age, co morbidities, vital signs, mental status, skin turgor and urine output.

Patients require pulse oximetry because one of the most common systemic complications is hypoxemia caused by acute lung injury. They should receive supplementary oxygen to maintain arterial saturation above 95%.

It is also essential to provide adequate analgesia. Narcotics are usually the preferred group of analgesics.

Nutritional support is vital in the treatment of acute pancreatitis. It has been shown that enteral nutrition has many benefits over total parenteral nutrition in severe acute pancreatitis. However, a meta-analysis showed that total enteral nutrition has no better advantage over total parenteral nutrition with respect to outcome.[25]

Role of antibiotics in pancreatitis is controversial. Recent meta-analyses have proven that prophylactic antibiotics do not decrease the frequency of surgical interventions, infected necrosis, or mortality in patients with severe pancreatitis. In addition, they are associated with gram positive cocci and candidal infections. Further, some meta- analyses conclude that the use of antibiotics prophylactically can reduce the infection, surgical rates and sepsis and in turn mortality. Thus, the use of prophylactic antibiotics for necrotizing pancreatitis must be weighed carefully with the benefits and risks.[25]

The role of Somatostatins and octreotide in acute pancreatitis is that, they inhibit both the basal and stimulated pancreatic secretion. They also stimulate reticuloendothelial system activity, modulate the cytokine cascade and are cytoprotective with respect to the pancreas.

These effects of somatostatin and octreotide suggest that both drugs may be useful either in the treatment of pancreatic disorders, or in preventing acute pancreatitis.

The role of surgery in acute pancreatitis includes debridement of the necrotic material in infected necrotizing pancreatitis and in clinically deteriorating patients with sterile necrosis. The timing of surgery is usually within two weeks of the onset of symptoms.

The indications for surgical intervention in necrotizing pancreatitis are:

- Diagnostic uncertainty
- Intra-abdominal catastrophe unrelated to necrotizing pancreatitis
- Infected necrosis documented by FNA or extraluminal gas on CT
- Severe sterile necrosis
- Symptomatic organized pancreatic necrosis

Surgical options for infected necrosis include:

- Minimally invasive management - necrosectomy

- Conventional management - necrosectomy with simple drainage
  - Closed lavage of the debrided cavity,
  - Closed management - necrosectomy with closed continuous postoperative lavage
  - Open management - necrosectomy with planned staged reoperations at definitive intervals with repeated lavage.

In case of Gall stone induced pancreatitis, early laparoscopic cholecystectomy is indicated in mild cases where cholecystetomy is done during the initial admission itself as it is a safe procedure and reduces recurrence. In severe case however, cholecystectomy is planned only after 6 weeks in order to reduce the stay.

The use of ERCP with sphincterotomy in pancreatitis is only indicated in:

- ✓ Severe acute biliary pancreatitis
- ✓ Those who develop cholangitis,
- ✓ Those with persistent bile duct obstruction and

- ✓ In older patients unfit for surgery.[8]

But the disadvantages associated with ERCP are:

- ✓ ERCP itself can precipitate pancreatitis and it can introduce infection to sterile pancreatitis
- ✓ The risk of bleeding is present

Role of Pancreatic resection in acute pancreatitis:

Ductal necrosis can result in the entity called disconnected duct syndrome, most commonly involving the mid pancreatic body along with the ductal epithelium. Disconnected pancreatic duct is an anatomic situation where there is a lack of ductal continuity between viable secreting pancreatic tissue and the gastrointestinal tract .The isolated viable pancreatic segment continues to have an exocrine output that is not drained into the bowel. The resultant fistula and inflammatory collections are persistent and are unlikely to resolve with conservative drainage measures, mandating surgical treatment.

The criteria for diagnosing disconnected duct syndrome include:

i) ERCP evidence of main pancreatic duct cut-off or discontinuity with inability to access or cannulate the upstream pancreatic duct;

ii) CT evidence of viable pancreatic tissue upstream from the pancreatic duct cut-off or discontinuity and

iii) A non healing pancreatic fistula, pseudocyst or fluid collection despite a course of conservative medical management.

Pancreatic duct leaks and fistulas occur at times in acute necrotizing pancreatitis. The damage to the pancreatic ductal system allows pancreatic juice to leak from the gland. Sudden development of hypocalcemia or a rapid increase in retroperitoneal fluid on CT scan is suggestive of this condition.

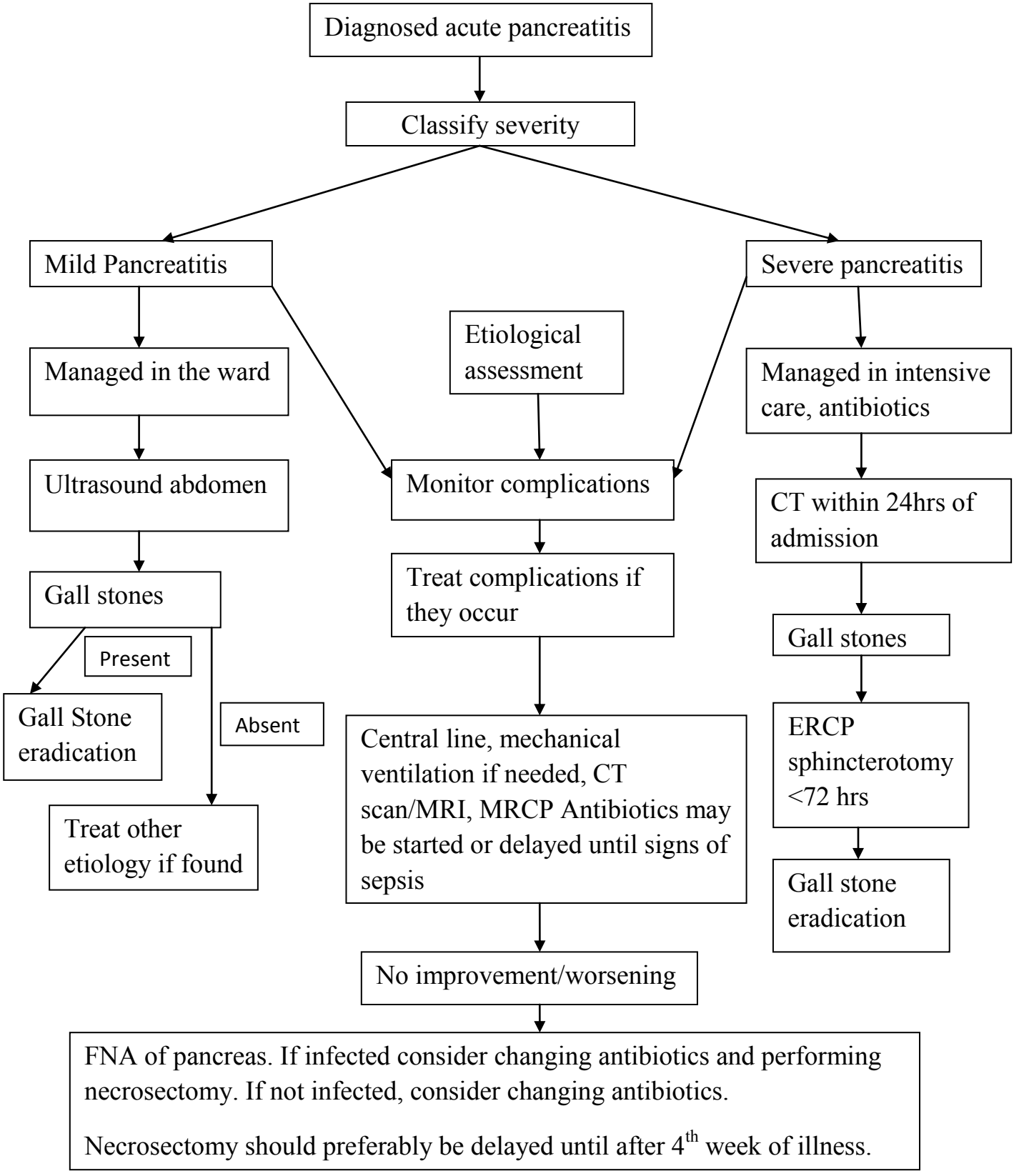
Ductal disruption following acute pancreatitis can result in pancreatic fluid collection or pseudocyst, pleural effusion, pancreatic ascites, pancreaticocutaneous fistulas and severe pancreatic necrosis. Main pancreatic ductal disruption causes continuous enzymatic insult to the pancreas and a disconnected gland syndrome.

Ductal disruption can be associated with a pancreatico-cutaneous fistula, especially after surgical necrosectomy or percutaneous drainage. If surgical necrosectomy is mandated in severe cases with infected necrosis, the percutaneous drainage of fluid collections should be avoided because it transforms a collection easily accessible to endoscopic drainage into a permanent fistula with a high rate of relapse, when the percutaneous drain is removed.

Refractory cases require surgery. In 1963, Watts described survival of a patient with pancreatitis who had been treated by total pancreatectomy approximately 48 hours after onset of symptoms.

- If the persistent leak is present in the tail of the gland, a distal pancreatectomy is preferred.
- If the leak is in the head of the gland, a Whipple procedure is the operation of choice.[26, 27, 28]

Fig 9: Algorithm for management of Acute Pancreatitis



MATERIALS AND METHODS

This prospective study was conducted in Department of General Surgery, Government Royapettah Hospital from January 2013 to July 2013 after obtaining permission from the Institution's Research and Ethical committee.

SOURCE OF DATA:

The study was conducted on sequential admission of 100 patients diagnosed with acute pancreatitis in Government Royapettah Hospital.

METHOD OF COLLECTION OF DATA:

- Patients with acute pancreatitis were diagnosed as per Atlanta symposium which is any two of the three findings:
  - Abdominal pain consistent with acute pancreatitis, i.e., severe and persistent epigastric pain, acute in onset, radiating to the back
  - Serum amylase or lipase: three or more times the normal limit (in our laboratory normal value of Sr. amylase- 50 – 150 SU/dL.

- CECT (Contrast Enhanced Computerized Tomography) findings characteristic with acute pancreatitis and less commonly with MRI or Ultrasonography of abdomen

⦿ Informed consent was obtained from patients for including them in my study

⦿ Blood samples were taken at the time of admission and sent for Serum Amylase, Sr. urea, Sr. creatinine and liver function test analysis

⦿ Similarly, Samples were sent for total WBC count and differential count

- At the time of admission
- At 24hrs
- At 48hrs

⦿ Neutrophilic lymphocytic ratio (NLR) was calculated which is the ratio of the Absolute Neutrophil count (in %) and Absolute Lymphocyte count (in %).

⦿ Appropriate tests were conducted like Sr. Creatinine, Blood Pressure monitoring and Spo2 as and when needed to look for features of organ failure.

- NLR values were correlated with the severity of pancreatitis as per Atlanta classification.

INCLUSION CRITERIA:

- All cases of acute pancreatitis admitted in our hospital from December 2012 to July 2013.

EXCLUSION CRITERIA:

- Patients with chronic pancreatitis

METHOD OF STATISTICAL ANALYSIS:

The NLR for day 0, day1 and day 2 for mild pancreatitis and severe pancreatitis were analyzed using independent sample t test. A ‚p' value of < 0.05 is indicated as statistically significant.

RESULTS

I) DEMOGRAPHIC DATA:

Of the admissions that were between December 2012 to July 2013, 100 patients with acute pancreatitis details were accumulated and results analyzed as follows.

Of the 100 patients, 80 patients had mild pancreatitis and 20 patients developed severe pancreatitis. Of the severe pancreatitis patients, 6 patients developed organ failure, 4 patients developed pseudocyst, 2 developed pancreatic abscess and 8 patients had organ failure. Of these patients, 4 of them died.

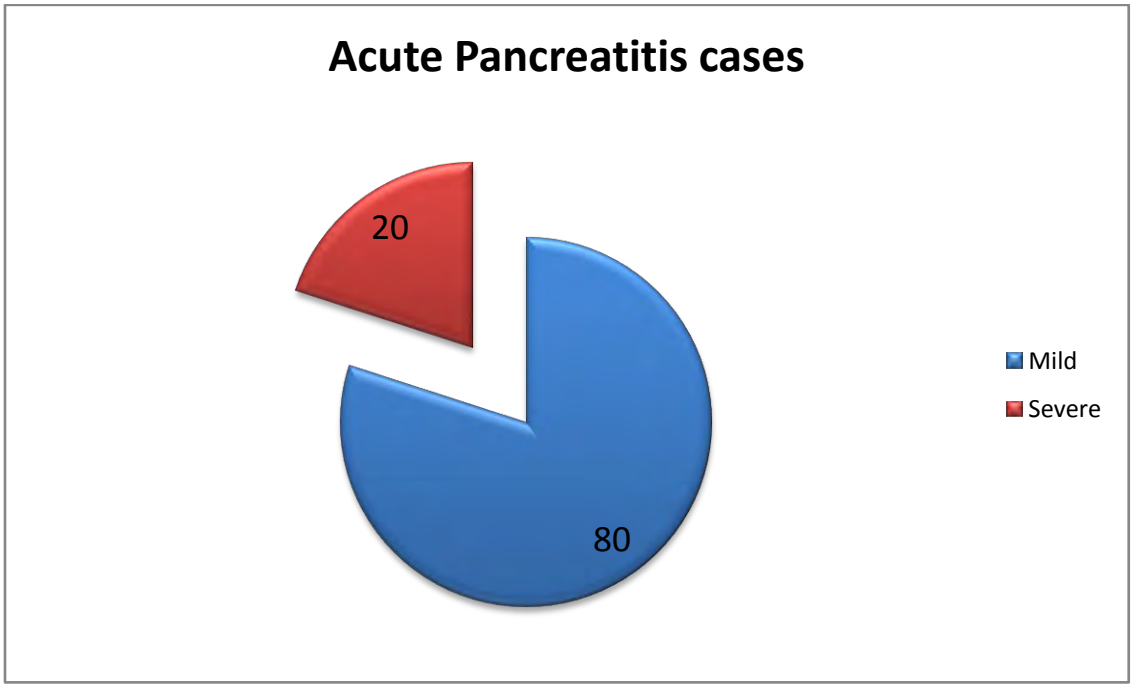
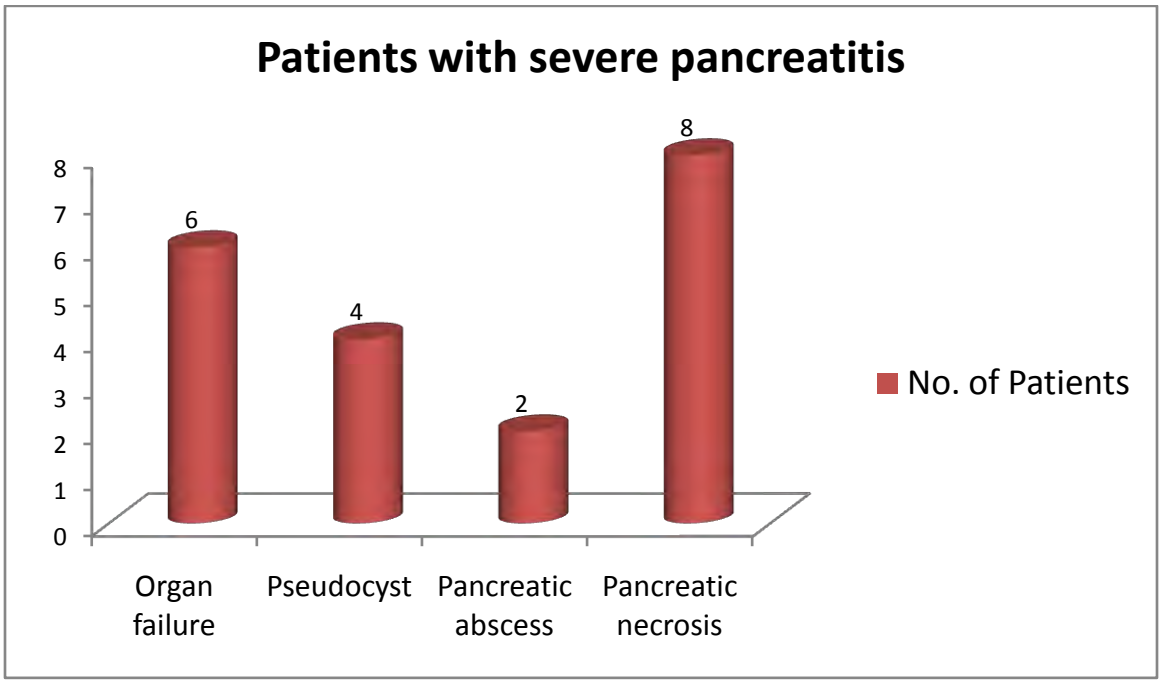


Chart 1: Mild vs. Severe Pancreatitis

Chart 2: Presentation of Severe pancreatitis



A. ***Age:***

Among the 100 patients it was noted that pancreatitis occurred more in the age group of 31-40 years. It can be seen that on calculating the percentage of severe pancreatitis among each group, it was highest in the 51-60yrs age group (50%).

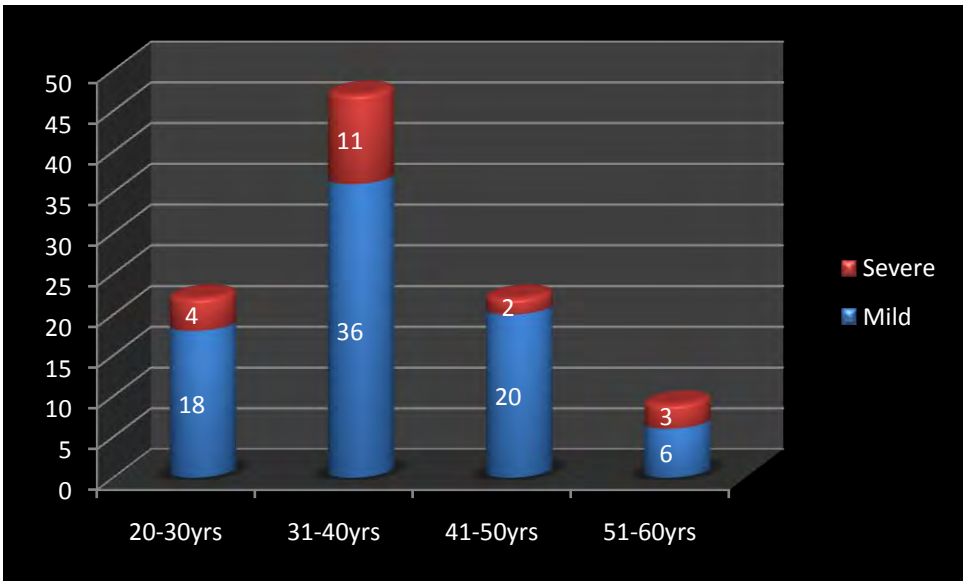


Chart 3: Age distribution

Among 100 patients, on comparing the sex distribution, in my study only 4 patients in acute pancreatitis were females.

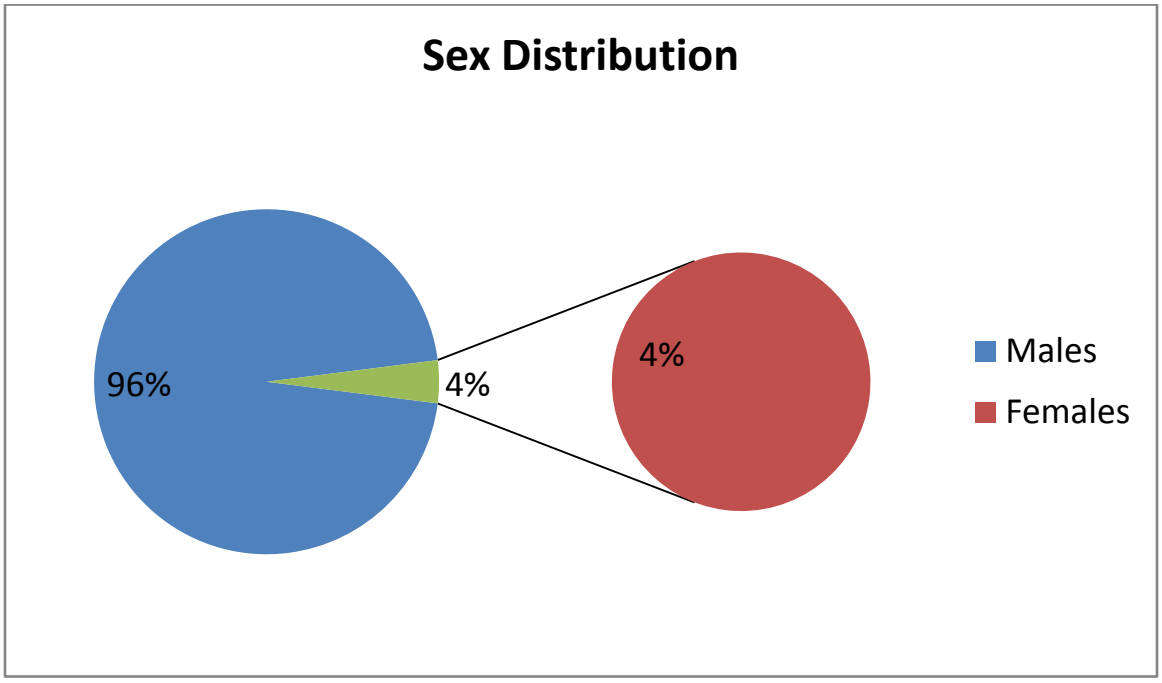


Chart 4: Sex Distribution

II) CLINICAL DATA:

The Total WBC count was significantly increased in severe pancreatitis group. The differential count were individually analyzed which is summarized as follows

A. ***Neutrophil count:***:

It was found that in my study the neutrophil count in both mild and severe pancreatitis was high on the day of admission. Over the next 48 hours, the neutrophil counts decreased in mild pancreatitis whereas, in severe pancreatitis group, the neutrophil count was persistently high.

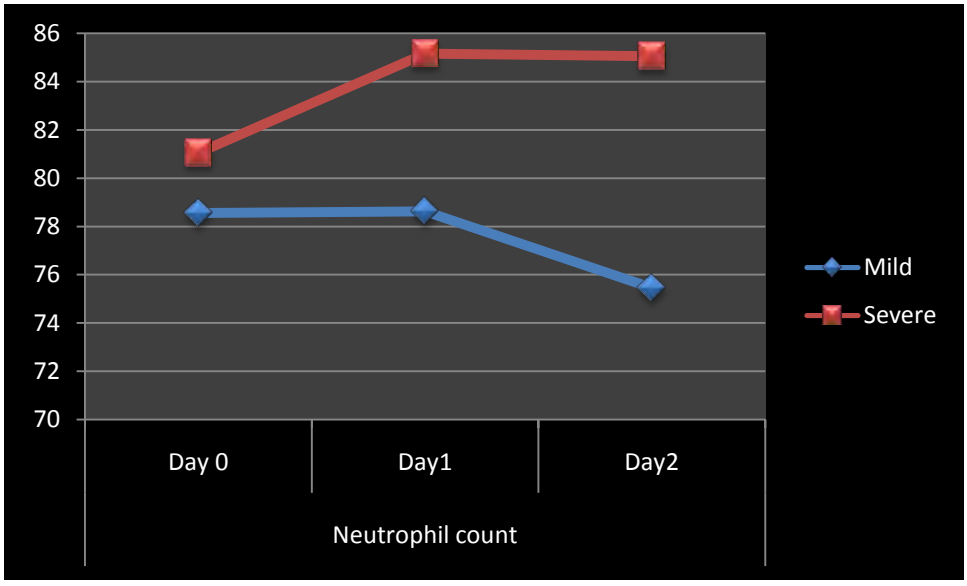
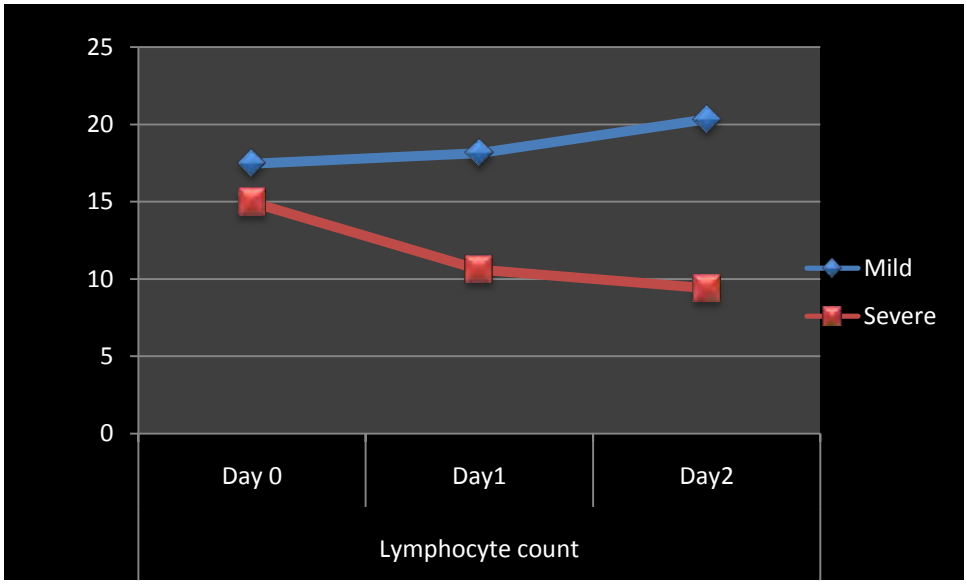


Chart 5: Trend of Neutrophil Count

B. ***Lymphocyte count:***

Both in mild and severe pancreatitis, the lymphocyte count were suppressed. Over, the next 48 hours, the counts started to rise in mild pancreatitis group whereas it started to fall further in severe pancreatitis group.

Chart 6: Trend of Lymphocyte Count

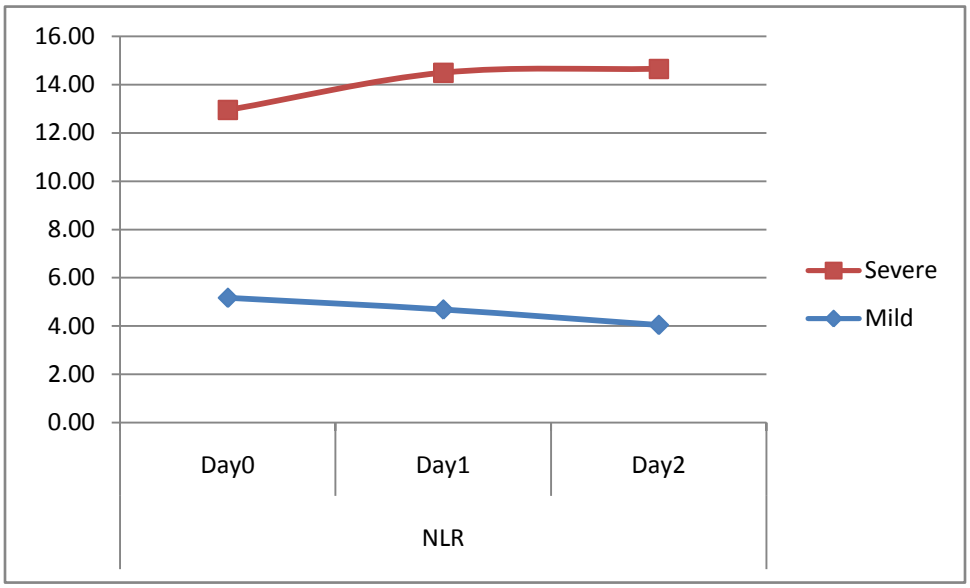


C. ***Neutrophilic lymphocytic ratio (NLR):***

As there was a change in the trend of neutrophils and lymphocytes over 48 hours, the NLR calculated over the 48 hours was analyzed and tabulated using independent sample t test. It was found that there was a statistically significant difference ($p< 0.05$) between the mild and severe pancreatitis group. The NLR was found to be significantly higher in severe pancreatitis group than the mild pancreatitis group. It

seemed to return to slightly fall in mild pancreatitis group, but it was persistently high and increasing in severe pancreatitis group.

Chart 7: Trend of NLR



Group Statistics

	Atlanta classfn	N	Mean	Std. Deviation	Std. Error Mean
day0	Mild	80	4.3849	1.44457	.16253
	Severe	20	8.2075	3.81838	.85382

Group Statistics

	Atlanta classfn	N	Mean	Std. Deviation	Std. Error Mean
day1	Mild	80	5.0749	1.92036	.21606
	Severe	20	9.0665	3.39489	.75912

Group Statistics

	Atlanta classfn	N	Mean	Std. Deviation	Std. Error Mean
day2	Mild	80	4.5182	1.86058	.20933
	Severe	20	10.8925	3.96859	.88740

NLR	**p value**	**95% confidence interval**
Day 0	**.000**	**5.63-2.01**
Day 1	**.000**	**5.62-2.35**
Day 2	**.000**	**8.26-4.47**

On applying the levene's test, it was found that the NLR was significantly increased in severe pancreatitis was significantly higher in severe pancreatitis group than the mild pancreatitis group.

DISCUSSION

In this study on 100 patients, acute pancreatitis was more predominant among Males (96%) than females (4%). This was similar to a study done by Rithin et al. in which pancreatitis was common among males.[29] Also it is comparable to a study by Savio G Barreto et al, where their male: female ratio was 96.1%: 3.9%.[30] This observation may be due to the reason that alcohol consumption is more common among males in a developing country like India.

In my study, most of the patients who presented with acute pancreatitis belonged to 31-40 yrs age group. The mean age was around 38.3% compared to the study by Rithin et al in which the mean age was 40.9%.[29] Similarly; mean age was 40yrs in a study by Savio G Barreto et al.[30]

In my study, the most common etiology was alcohol which was around 98% as compared to study by Savio G Barreto et al, where alcohol was the causative agent in 92.6% and gallstones in

19%.[30] In another study by Kimmo et al, alcohol was accounted to 79 % and gall stones to 13%.[31]

Of the 100 patients, 80% of them had mild pancreatitis and 20% had severe pancreatitis as compared to study by Savio G Barreto et al, 67 % had mild and 33% had severe disease.[30] My study seems comparable to the rate of incidence of mild and severe pancreatitis as per Atlanta symposium, in which the rate of mild pancreatitis is 70-80 % and 20-30 % in severe pancreatitis patients.

In my study, mortality rate 4% as compared to a mortality rate of 12% by Savio G Barreto et al.[30]

In my study I also noticed that, serum amylase was elevated (≥ 3times the normal) in only 37 patients while it was < 3 times the normal in 63 patients. This was in contrast to the diagnostic criteria proposed by the Atlanta. When analyzed, there were studies which showed lower levels of amylase in patients with acute pancreatitis and severe destruction of the pancreas. Winslet et at reported that patients with low enzyme levels more frequently had associated pancreatic necrosis. Lankisch P G et al in his study suggested that

we should not depend on elevated enzyme levels of >3n for diagnosis. Also they reported that it was especially true in pancreatitis caused by alcohol, where the amylase level was lower at the time of admission. As alcohol induced pancreatitis was the major cause in my study group the lower amylase values may be attributable to it.[32]

The primary finding in my study is that the Neutrophilic Lymphocytic Ratio (NLR) was elevated in patients presenting with acute pancreatitis. The NLR was increased when compared to the normal (2.63).[34]

The WBC count is a marker of infection and inflammation. It is a part of many scoring systems used to prognosticate acute pancreatitis. The two important components of WBC are the neutrophils and lymphocytes. In acute pancreatitis inflammatory cytokines like TNF-α are responsible for recruitment of neutrophils and macrophages into the pancreatic tissue. The neutrophils in turn propagate inflammation and tissue destruction through proteolytic enzymes (myeloperoxidase, elastase, collagenase and β-

glucoronidase), cytokines (IL6, IL8, TNF-α) and oxygen free radicles. As the severity of pancreatitis increases, there is progression to Systemic Inflammatory Response (SIRS) and Multi Organ Dysfunction Syndrome (MODS) and this corresponds with the increase in neutrophil numbers.

This was clearly elicited in my study where the neutrophil count progressively increased in severe pancreatitis group, where there was progression to SIRS. In contrast, in mild pancreatitis, as the disease severity decreased, the neutrophil count also started to decline toward normalcy.

Lymphocyte numbers increase following the initial stress and mediate the subsequent inflammatory response. The previous view is that neutrophilia is the primary cause of an elevated NLR, SIRS and poor prognosis, while lymphocyte count remains constant. However in my study, as per (chart 6) there was lymphopenia within 24hrs of admission which was persistent in severe pancreatitis group than the mild group and hence contributing to the increased NLR.

This persistent lymphopenia has been attributed to progressive inflammation, bacteremia or sepsis in intensive care patients in other studies.[24] Uncontrolled inflammation is thought to precipitate lymphopenia by redistribution of lymphocytes, accelerated apoptosis and hence lymphopenia responsible for higher mortality in patients with septic shock.

Similar to my study, Pezzilli et al who compared patients of acute pancreatitis with other acute abdominal conditions, reported a lymphopenia on day 1 in acute pancreatitis patients which persisted on days 3 and 5 following admission.[24]

Similarly, Takeyama in his study noted that lymphocytes were significantly lower in severe pancreatitis patients who subsequently developed infective complications. Further, they noticed that it was the CD 8 positive lymphocytes which underwent apoptosis leading to impaired cellular immunity and in turn to infective complications.

It is this varying trend of neutrophils and lymphocytes that led to the proposal of assessing the neutrophilic lymphocytic ratio

as a predictive and a single factor than either of the component alone.

The Neutrophilic Lymphocytic Ratio has been evaluated in many benign and malignant conditions and a high NLR has been associated with poor outcome. A study was done which evaluated NLR in acute coronary syndrome and reported that an elevated NLR predicted in-hospital death and 6-month mortality. It was also associated with early hospital death and heart failure following myocardial infarction.

Similarly, NLR was evaluated in predicting cancer recurrence, disease free survival in patients with Hepatocellular cancer (HCC) and colorectal liver metastasis who underwent surgery and found that an elevated NLR was associated with a poor outcome.

NLR has been shown to reflect SOFA (Sequential Organ Failure Assessment) and APACHE II scores in patients in intensive care setting. It is these scores which are also used in

predicting severity in acute pancreatitis. So, NLR has been evaluated in predicting the severity in acute pancreatitis.

In my study, Neutrophilic Lymphocytic Ratio was assessed between mild and severe pancreatitis on day0, day1 and day 2 of admission. As per (chart 7), the NLR seems to represent a dynamic process where in it tends to return to normalcy in mild pancreatitis whereas it s persistently high in severe acute pancreatitis.

The difference in NLR pattern between the mild and severe acute pancreatitis was analyzed by independent sample t test and was found to be statistically significant ($p < 0.05$).

This variation in NLR was analyzed by Suppiah A et al and they reported that NLR was raised significantly in poor prognosis group than the favourable group. In their study the NLR was comparable at baseline that is at the time of admission. The NLR then gradually returned towards normal in favourable group while was persistently high in the poor prognosis group which is similar to my study.

Similar study was conducted by Azab et al and they reported NLR to be superior to the total WBC count or individual neutrophil and lymphocyte counts in predicting ICU admission and death in acute pancreatitis patients. They further proceeded and recommended a cut-off value of ≥ 4.7 to identify poor outcome in acute pancreatitis.[33]

Another study conducted by Vedat goral et al in acute pancreatitis also reported that the leukocyte/ lymphocyte ratio is a simple test to indicate the severity of the disease.[34]

The benefit of my study is that NLR can be calculated by just doing a total WBC and a differential count. In comparison to other severity scoring systems, where there are multiple parameters required to calculate the prognosis, NLR analysis just needs a single blood test needs to be done serially.

In some systems like the Ranson's and glascow scoring systems which can be calculated only after 48hrs of admission, the crucial period in management of acute pancreatitis is lost leading to a worse prognosis. In my study, NLR can be done at the time of

admission and can be serially monitored which can act as a guide to detect those patients progressing to severe pancreatitis. Those patients progressing to severe pancreatitis can be identified earlier and can be managed intensively and hence reduce the morbidity and mortality.

NLR is a cost effective, simple tool which can be calculated in any level care of hospital be it a secondary care or a tertiary care hospital. India being a developing country has a low Doctor: Patient ratio and limited facilities are available at the peripherally located hospitals. With alcohol induced pancreatitis being more common among the low socioeconomic status, multiple blood tests would be a burden for them. In that case, differential WBC count would be a cheaper and an easier blood test that can be performed and the NLR thus calculated can be used as a guide to refer poor prognosis patients to a higher center for intensive care and management.

CONCLUSION

In my study, Neutrophilic Lymphocytic Ratio has proved to be a single indicator in assessing the severity of acute pancreatitis.

NLR can be easily calculated and is a routine workup investigation that is done in all patients at the time of admission. Being a routine investigation, it bears no additional cost to the patient.

NLR seems to correlate well with the severity and outcome of acute pancreatitis. Continuous monitoring on each day will provide a dynamic reflection of the immunity and inflammatory response of the body to pancreatitis and hence predict the prognosis earlier.

NLR assessment trespasses the limitation of Ranson's scoring system that, it can be used at the time of admission itself and monitoring is possible in the first 48 hours. It covers the limitation of APACHE II scoring system in a way that it avoids multiple parameters needed for assessment. However, as of now APACHE II is considered the most useful the most useful test to predict severity.

Still further studies need to be performed to find out if we can predict an optimal Neutrophilic Lymphocytic Ratio which can delineate mild pancreatitis and those progressing to severe pancreatitis.

As of now, only the study by Azab et al has proposed a neutrophil lymphocyte ratio value of ≥ 4.7 in predicting the severity in acute pancreatitis.[33] However, as per Suppiah et al, this value has a high sensitivity (90.9 %) but a low specificity (22 %).[24]

So, Future studies are needed which can optimize the NLR and investigate if its incorporation would increase the accuracy of the current Acute pancreatitis prognostic scoring systems.

SUMMARY

Acute pancreatitis is still one of the most common causes of emergency hospital admissions in India. The overall mortality due to acute pancreatitis has remained 10-15% in the past 20 years. Accurate predictors of the severity of acute pancreatitis are important because they influence clinical decision making. In this study, we evaluated 100 patients of acute pancreatitis and we found that pancreatitis is more common in males and alcohol being most common etiological factor.

Neutrophilic Lymphocytic Ratio (NLR) was calculated among these patients and was found to be increased in acute pancreatitis. It was significantly higher in severe pancreatitis patients than the mild pancreatitis patients.

The NLR seems to persistently rise in poor prognostic patients when it was serially calculated. Hence, it is a dynamic indicator of the severity of the disease.

NLR can be easily assessed. It can be calculated from a blood test which is routinely done for all patients at the time of admission. It is thus a cost effective tool.

NLR is a simple, single indicator of the prognosis of pancreatitis which would help in providing aggressive treatment to those patients progressing to severe pancreatitis.

Future studies are needed which would incorporate this NLR into the current scoring systems and thus increase their accuracy.

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ANNEXURES

INSTITUTIONAL ETHICAL COMMITTEE
GOVT.KILPAUK MEDICAL COLLEGE,
CHENNAI-10
Ref.No.5614/ME-1/Ethics/2013 Dt:04.07.2013
CERTIFICATE OF APPROVAL

The Institutional Ethical Committee of Govt. Kilpauk Medical College, Chennai reviewed and discussed the application for approval "A Study of neutrophilic lymphocytic ratio as a prognostic factor in acute pancreastic" – For Research Work submitted by Dr.H.Divya Devi, MS (GS), PG Student, GRH, Chennai.

The Proposal is APPROVED.

The Institutional Ethical Committee expects to be informed about the progress of the study any Adverse Drug Reaction Occurring in the Course of the study any change in the protocol and patient information /informed consent and asks to be provided a copy of the final report.

GOVT. KILPAUK MEDICAL COLLEGE * Kilpauk, Chennai-10. * 09 OCT 2013

9/10/13.
CHAIRMAN,
Ethical Committee
Govt.Kilpauk Medical College,
Chennai

15/7

SL NO	NAME	AGE	SEX	IP NO.	DAY 0			DAY 1			DAY 2			AMYL	USG/CT FINDING	ATLANTA CLASSIFICATION
					TC/DC		NLR	TC/DC		NLR	TC/DC		NLR			
1	SHANKAR	32	M	13103	6200		2.03	10800		2.39	8600		2.46	224	ACUTE PANCREATITIS WITH ASCITES	MILD
					65	32 3		67	28 5		69	28 3				
2	MANOHARAN	48	M	7029	10800		3.57	8800		2.46	8600		2.39	413	ACUTE PANCREATITIS	MILD
					75	21 4		69	28 3		67	28 5				
3	ANBU	50	M	19199	10300		3.33	8500		2.18	8500		2.42	568	ACUTE PANCREATITIS WITH FLUID COLLECTION HEAD OF PANCREAS	MILD
					70	21 9		61	28 2		63	26 2				
4	ANBU	50	M	20836	14000		2.59	11800		2.59	10600		2.39	339	ACUTE PANCREATITIS WITH ASCITES	MILD
					70	27 3		70	27 3		67	28 5				
5	SARAVANAN	36	M	5998	6800		1.62	6800		2.03	7600		2.39	169	ACUTE PANCREATITIS WITH RETROPERITONEAL FASCIAL INFLAMMATION	MILD
					60	37 3		65	32 3		67	28 5				
6	LEELAIHARAN	38	M	20835	7100		2.77	6500		5.00	5800		9.56	461	DIFFUSELY ENLARGED HYPOECHOIC PANCREAS ACUTE PANCREATITIS	SEVERE
					72	26 2		80	16 4		86	9 5				
7	ANAND	27	M	20373	6300		5.13	7000		3.33	7200		1.62	339	ACUTE PANCREATITIS WITH LEFT PLEURAL EFFUSION	MILD
					82	16 2		70	21 21		60	37 3				
8	MURUGAN	38	M	18988	9900		4.44	8600		3.33	8000		2.18			
					80	18 2		70	21 9		61	28 2		297	ACUTE PANCREATITIS	MILD
9	RAJA	40	M	17948	10800		3.57	8600		3.33	6700		2.39	447	ACUTE PANCREATITIS	MILD
					75	21 4		70	21 9		67	28 5				

SL NO	NAME	AGE	SEX	IP NO.	DAY 0				DAY 1				DAY 2				AMYL	USG/CT FINDING	ATLANTA CLASSIFICATION
					TC/DC			NLR	TC/DC			NLR	TC/DC			NLR			
10	BASKAR	31	M	9316	7900			1.45	7800			2.00	7700			2.52	365	ACUTE PANCREATITIS WITH PSEUDOCYST PANCREAS	SEVERE
					58	40	2		66	33	4		68	27	5				
11	KRISHNA MOORTHY	52	M	9391	5800			1.57	6300			5.13	6300			9.56	206	ACUTE FLUID COLLECTION WITH ASCITES	SEVERE
					58	37	3		82	16	2		86	9	5				
12	SAKTHIVEL	35	M	10373	6800			1.88	9900			4.44	8600			5.13	155	ACUTE PANCREATITIS WITH PSEUDOCYST	SEVERE
					64	34	2		80	18	2		82	16	2				
13	ANNADURAI	38	M	10311	6600			1.35	8600			3.33	6700			2.39	365	ACUTE PANCREATITIS	MILD
					54	40	6		70	21	9		67	28	5				
14	SATYA	52	M	5158	7400			1.77	8100			3.33	8000			2.39	218	ACUTE PANCREATITIS PERIPANCREATIC INFLAMMATION	MILD
					62	35	3		70	21	9		67	28	5				
15	THAMEEM ANSARI	30	M	7093	9200			2.46	8500			2.92	5600			3.33	292	ACUTE PANCREATITIS	MILD
					69	28	3		76	26	8		70	21	9				
16	SELVAM	38	M	2948	12600			9.56	12000			10.0	11600			11.0	317	ACUTE NECROTISING PANCREATITIS WITH ABSCESS	SEVERE
					86	9	5		90	9	1		88	8	4				
17	RAJI	25	M	19158	8400			3.33	7800			3.57	6500			2.46	486	ACUTE PANCREATITIS	MILD
					70	21	9		75	21	4		69	28	3				
18	ANTHONY	38	M	17278	7800			3.57	7500			3.89	6800			3.33	380	ACUTE PANCREATITIS	MILD
					75	21	4		74	19	7		70	21	9				
19	MUNUSAMY	40	M	6652	8600			6.46	10600			11.00	11400			13.8	570	ACUTE PANCREATITIS WITH NECROSIS	SEVERE
					84	13	3		88	8	4		83	6	11				

SL NO	NAME	AGE	SEX	IP NO.	DAY 0			DAY 1			DAY 2			AMYL	USG/CT FINDING	ATLANTA CLASSIFICATION
					TC/DC		NLR	TC/DC		NLR	TC/DC		NLR			
20	POIYAMANI	34	M	21150	8900		4.44	8600		3.57	7800		3.41	361	ACUTE PANCREATITIS	MILD
					80	18 2		75	21 4		75	22 3				
21	RAVI	30	M	19280	9200		3.90	9400		4.21	8200		3.62	421	ACUTE PANCREATITIS WITH ASCITES	MILD
					78	20 2		80	19 1		76	21 3				
22	BABU	41	M	19217	8200		3.62	8600		3.57	7800		3.57	510	ACUTE PANCREATITIS	MILD
					76	21 3		75	21 4		75	21 4				
23	NAGARAJ	35	M	18081	7800		4.21	8400		5.00	7800		3.90	551	ACUTE PANCREATITIS	MILD
					80	19 1		80	16 4		78	20 2				
24	JOSEPH	25	M	15756	7400		3.90	8400		4.21	6800		3.57	487	ACUTE PANCREATITIS	MILD
					78	20 2		80	19 1		75	21 4				
25	MUTHU MANICKAM	30	M	9918	9200		7.00	8200		8.20	7400		7.50	361	ACUTE PANCREATITIS WITH FLUID COLLECTION	MILD
					84	12 4		82	10 8		75	10 15				
26	AYYANAR	26	M	9375	6800		5.13	7200		4.44	8200		3.57	468	ACUTE PANCREATITIS	MILD
					82	16 2		80	18 2		75	21 4				
27	VENKATESH	37	M	9264	5800		6.46	9600		5.86	9800		5.13	471	ACUTE PANCREATITIS WITH ASCITES	MILD
					84	13 5		82	14 4		82	16 2				
28	MANOHARAN	48	M	7029	10800		3.57	11000		3.62	10200		3.90	268	ACUTE PANCREATITIS	MILD
					75	21 4		76	21 3		78	20 2				
29	DILLIBABU	38	M	10696	11600		4.82	11800		13.8	10600		22.0	615	ACUTE NECROTISING PANCREATITIS	SEVERE
					82	17 11		83	6 11		88	4 5				
30	MARY	34	F	17656	10800		3.33	8600		2.39	10200		2.77	357	ACUTE PANCREATITIS	MILD
					70	21 9		67	28 5		72	26 2				

SL NO	NAME	AGE	SEX	IP NO.	DAY 0			DAY 1			DAY 2			AMYL	USG/CT FINDING	ATLANTA CLASSIFICATION
					TC/DC		NLR	TC/DC		NLR	TC/DC		NLR			
31	THARANIVELU	60	m	95413	9600		4.21	7400		6.33	7900		3.90	457	ACUTE PANCREATITIS	MILD
					80	19 1		76	12 3		78	20 2				
32	OMPRAKASH	40	M	91129	7800		3.57	10600		4.21	9700		3.62	513	ACUTE PANCREATITIS WITH ASCITES	MILD
					75	21 4		80	19 1		76	21 3				
33	BABU	28	M	8284	6800		11.0	12300		12.6	11800		11.7	719	ACUTE NECROTISING PANCREATITIS	SEVERE
					88	8 4		88	7 5		82	7 11				
34	NELSON	40	M	3422	7600		6.46	6800		5.13	9600		3.90	415	ACUTE PANCREATITIS	MILD
					84	13 3		82	16 2		78	20 2				
35	SATYA	50	M	5159	8700		4.44	7800		3.62	9000		3.33	371	ACUTE PANCREATITIS	MILD
					80	18 2		76	21 3		70	21 4				
36	KALAIARASAN	35	M	650	5600		2.77	7700		2.39	4100		2.03	365	ACUTE PANCREATITIS WITH ASCITES	MILD
					72	26 2		67	28 3		65	32 3				
37	SELVAM	38	M	2843	7800		7.50	6100		5.86	6200		6.46	513	ACUTE PANCREATITIS WITH FLUID COLLECTION	MILD
					75	10 15		82	14 4		84	13 3				
38	SUDHAKAR	26	M	3025	12700		10.0	13500		10.3	7500		9.56	625	ACUTE PANCREATITIS WITH PSEUDOCYST	SEVERE
					90	9 1		82	8 10		86	9 5				
39	VENKAT	41	M	519	4300		2.63	5400		3.62	5100		3.33	484	RESOLVING PANCREATITIS	MILD
					71	27 2		76	21 3		70	21 9				
40	DOWLAY	43	M	10814	8200		5.00	9500		3.57	4700		2.46	371	ACUTE PANCREATITIS	MILD
					80	16 4		75	21 4		69	28 3				
41	MURUGESAN	40	M	10993	7600		3.90	6700		3.89	9400		2.77	461	ACUTE PANCREATITIS	MILD
					78	20 2		74	19 7		72	26 2				

SL NO	NAME	AGE	SEX	IP NO.	DAY 0			DAY 1			DAY 2			AMYL	USG/CT FINDING	ATLANTA CLASSIFICATION
					TC/DC		NLR	TC/DC		NLR	TC/DC		NLR			
42	RAGAVAN	44	M	10797	8600		4.56	7900		4.21	8800		4.44	375	ACUTE PANCREATITIS	MILD
					82	18 0		80	19 1		80	18 2				
43	SELVAKUMAR	37	M	10731	9800		5.93	10200		6.23	11000		6.31	380	ACUTE PANCREATITIS WITH ASCITES	SEVERE
					83	14 3		81	13 6		82	13 5				
44	DILLIBABU	38	M	10696	12800		11.71	13600		12.6	13800		13.8	514	ACUTE NECROTISING PANCREATITIS	SEVERE
					82	7 11		88	7 5		83	6 11				
45	ANAND	37	M	10483	7800		7.50	8600		5.13	9200		4.44	475	ACUTE PANCREATITIS	MILD
					75	10 15		82	16 2		80	18 2				
46	KANNAN	39	M	5955	9600		5.93	10400		4.75	9800		4.56	416	ACUTE PANCREATITIS	MILD
					83	14 3		76	16 6		82	18 0				
47	UDHAYA KUM	27	M	5192	10400		6.31	9400		5.60	10200		5.13	518	ACUTE PANCREATITIS	MILD
					82	13 5		84	15 1		82	16 2				
48	ROSE	50	M	4215	9600		5.13	9800		5.00	10400		5.47	564	ACUTE PANCREATITIS	MILD
					82	16 2		80	16 4		82	15 3				
49	ANBARASAN	40	M	996	11200		6.62	10400		6.83	9800		5.3	487	ACUTE PANCREATITIS	MILD
					86	13 1		82	12 6		80	15 5				
50	ANAND	26	M	20373	7800		4.44	8200		3.57	7900		4.21	587	ACUTE PANCREATITIS	MILD
					80	18 2		75	21 4		80	19 1				
51	SHANKAR	29	M	20791	8400		6.23	8300		3.90	7900		4.44	483	ACUTE PANCREATITIS	MILD
					81	13 6		78	20 2		80	18 2				
52	SEAGU	32	M	19600	6400		3.57	400		2.46	6600		3.24	247	ACUTE PANCREATITIS	MILD
					75	21 4		69	28 3		68	21 1				

SL NO	NAME	AGE	SEX	IP NO.	DAY 0				DAY 1				DAY 2				AMYL	USG/CT FINDING	ATLANTA CLASSIFICATION
					TC/DC			NLR	TC/DC			NLR	TC/DC			NLR			
53	NATRAJ	52	M	19551	11600			9.56	12400			11.0	18400			12.6	630	ACUTE PANCREATITIS WITH PANCREATIC ABSCESS	SEVERE
					86	9	5		88	8	4		88	7	5				
54	RAGHU	37	M	19508	10800			7.50	9600			5.13	7500			3.89	213	ACUTE PANCREATITIS	MILD
					75	10	15		82	16	2		74	19	7				
55	PONNUSAMY	40	M	17965	11000			6.31	10300			5.86	9800			4.21	245	ACUTE PANCREATITIS	MILD
					82	13	5		82	14	4		80	19	1				
56	SHEEK	37	F	16898	10400			6.23	9800			5.19	10700			4.71	315	ACUTE PANCREATITIS	MILD
					81	13	6		83	16	1		80	17	3				
57	SUGUMAR	33	M	15399	11200			10.0	12800			9.56	10800			8.20	245	ACUTE PANCREATITIS WITH FLUID COLLECTION	MILD
					90	9	1		86	9	5		82	10	8				
58	ROSEMARY	40	F	15912	11800			5.86	7400			4.44	6600			3.33	413	ACUTE PANCREATITIS	MILD
					82	14	4		80	18	2		70	21	9				
59	RAMSINGH	56	M	14402	11600			3.57	10800			2.46	9800			2.03	467	ACUTE PANCREATITIS	MILD
					75	21	4		69	28	3		65	32	3				
60	RAJA	22	M	14251	8600			6.46	9400			5.13	8700			4.21	415	ACUTE PANCREATITIS	MILD
					84	13	3		82	16	2		80	19	1				
61	SUNDARAPAN	24	M	13881	10600			9.56	12400			10.0	11400			11.0	679	ACUTE PANCREATITIS WITH RENAL FAILURE	SEVERE
					86	9	5		90	9	1		88	8	4				
62	HUSSAIN	40	M	13887	7800			6.83	8200			5.53	9600			4.21	345	ACUTE PANCREATITIS	MILD
					82	12	6		83	15	2		80	19	1				
63	SIVAKUMAR	43	M	13685	9800			7.00	10200			6.46	11100			6.23	274	ACUTE PANCREATITIS	MILD
					84	12	4		84	13	3		81	13	6				

SL NO	NAME	AGE	SEX	IP NO.	DAY 0				DAY 1				DAY 2				AMYL	USG/CT FINDING	ATLANTA CLASSIFICATION
					TC/DC			NLR	TC/DC			NLR	TC/DC			NLR			
64	JAYAPAL	27	M	12368	7400			4.56	6600			4.75	6800			4.44	276	ACUTE PANCREATITIS	MILD
					82	18	0		76	16	6		80	18	2				
65	DURAI	56	M	13171	8900			6.46	6700			6.31	7400			6.23	213	ACUTE PANCREATITIS	MILD
					84	13	3		82	13	5		81	13	6				
66	SEBASTIAN RA	26	M	12668	9800			7.50	8600			6.83	7800			3.24	317	ACUTE PANCREATITIS	MILD
					75	10	15		82	12	6		68	21	1				
67	RAMDAS	36	M	12223	10100			4.21	7900			3.90	8200			3.60	148	ACUTE PANCREATITIS	MILD
					80	19	1		78	20	2		72	20	8				
68	RAJENDRAN	57	M	11705	9600			4.82	8600			12.6	8400			11.0	468	ACUTE PANCREATITIS WITH ARDS	SEVERE
					82	17	11		88	7	5		88	8	4				
69	VEERAMANI	34	M	10880	10000			8.70	11000			9.78	11600			10.0	461	ACUTE NECROTISING PANCREATITIS WITH GB SLUDGE	SEVERE
					87	10	3		88	9	3		90	9	1				
70	SHANTHAKUM	30	M	11664	6800			6.83	6600			6.31	6600			5.9	315	ACUTE PANCREATITIS	MILD
					82	12	6		82	13	5		83	14	3				
71	DURAI	47	M	11407	7400			5.13	7800			3.62	6800			3.6	461	ACUTE PANCREATITIS	MILD
					82	16	2		76	21	3		75	21	4				
72	RAMESH	31	M	11381	8600			8.20	9200			7.00	7800			4.2	264	ACUTE PANCREATITIS	MILD
					82	10	8		84	12	4		80	19	1				
73	AYATH BASHA	52	M	10953	10400			6.46	9600			5.13	9800			4.4	313	ACUTE PANCREATITIS	MILD
					84	13	3		82	16	2		80	18	2				
74	AUGUSTIN	48	M	10920	11200			9.56	11100			8.20	10800			7.5	415	ACUTE PANCREATITIS	MILD
					86	9	5		82	10	8		75	10	15				

SL NO	NAME	AGE	SEX	IP NO.	DAY 0			DAY 1			DAY 2			AMYL	USG/CT FINDING	ATLANTA CLASSIFICATION
					TC/DC		NLR	TC/DC		NLR	TC/DC		NLR			
75	THANGARAJ	38	M	10450	12600		11.7	11900		12.57	12200		10.0	597	ACUTE NECROTISING PANCREATITIS	SEVERE
					82	7 11		88	7 5		90	9 1				
76	POONGAVANA	46	M	10065	9700		4.56	8600		5.19	8700		5.1	275	ACUTE PANCREATITIS	MILD
					82	18 0		83	16 1		82	16 2				
77	ALIM	40	M	10482	10200		7.33	9800		6.23	9600		2.8	148	ACUTE PANCREATITIS	MILD
					88	12 0		81	13 6		72	26 2				
78	THANGAVEL	40	M	10421	13100		13.8	12700		14.83	11400		12.6	754	ACUTE HEMORRHAGIC PANCREATITIS	SEVERE
					83	6 11		89	6 5		88	7 5				
79	KALAISELVAN	30	M	10299	7600		7.08	6800		6.23	8700		5.9	245	ACUTE PANCREATITIS	MILD
					85	12 3		81	13 6		83	14 3				
80	RAJESH	37	M	10521	9900		8.20	8900		6.54	8600		5.5	218	ACUTE PANCREATITIS	MILD
					82	10 8		85	13 2		83	15 2				
81	SUNDAR	35	M	10279	10600		6.54	10000		5.60	11000		6.1	283	ACUTE PANCREATITIS	MILD
					85	13 2		84	15 1		86	14 0				
82	JAGAN	40	M	10270	11600		8.00	11500		4.69	10200		3.3	473	ACUTE PANCREATITIS	MILD
					88	11 1		75	16 9		76	23 1				
83	JAIGANESH	42	M	10014	10300		3.95	9800		5.06	8700		4.8	297	ACUTE PANCREATITITS	MILD
					79	20 1		81	16 3		76	16 6				
84	CHANDRAN	40	M	9980	9600		7.27	9700		5.47	9400		5.1	260	ACUTE PANCREATITIS	MILD
					80	11 9		82	15 3		82	16 2				
85	RAMADOSS	46	M	9723	8600		5.47	7900		3.33	6800		3.7	350	ACUTE PANCREATITIS	MILD
					82	15 3		70	21 9		77	21 2				

SL NO	NAME	AGE	SEX	IP NO.	DAY 0			NLR	DAY 1			NLR	DAY 2			NLR	AMYL	USG/CT FINDING	ATLANTA CLASSIFICATION
					TC/DC				TC/DC				TC/DC						
86	RAJA	21	M	9769	9500			4.59	9200			5.13	9100			4.9	394	ACUTE PANCREATITIS WITH ASCITES	MILD
					78	17	5		82	16	2		79	16	5				
87	KRISHNAN	54	M	9513	7500			9.11	7300			6.67	7100			0.2	439	ACUTE PANCREATITIS	MILD
					82	9	9		80	12	8		4	18	2				
88	MUTHUKUMA	21	M	9040	8600			7.08	8500			6.58	7900			5.1	393	ACUTE PANCREATITIS	MILD
					85	12	3		79	12	1		82	16	2				
89	SYED BUHARI	45	M	9012	11700			9.00	12200			9.56	12100			8.5	785	ACUTE NECROTISING PANCREATITIS	SEVERE
					90	10	0		86	9	5		85	10	5				
90	RAVI	48	M	8584	9500			5.60	8900			5.53	9000			4.7	245	ACUTE PANCREATITIS	MILD
					84	15	1		83	15	2		80	17	3				
91	NARAYANAN	50	M	8801	9300			9.67	9100			10.00	11200			11.0	746	ACUTE PANCREATITIS WITH PSEUDOCYST	SEVERE
					87	9	4		90	9	1		88	8	4				
92	KUMAR	32	M	8361	10200			2.71	9900			3.04	9600			3.0	245	ACUTE PANCREATITIS	MILD
					76	28	6		79	26	5		72	24	4				
93	KUPPAN	45	M	7069	9800			5.60	8800			5.93	7800			4.4	243	ACUTE PANCREATITIS	MILD
					84	15	1		83	14	3		80	18	2				
94	PALANI	40	M	7066	8700			6.08	8900			5.60	9200			5.2	336	ACUTE PANCREATITIS	MILD
					79	13	8		84	15	1		83	16	1				
95	SIVASHANKAR	27	M	7047	8100			2.39	9200			3.84	7400			3.6	426	ACUTE PANCREATITIS	MILD
					67	28	5		73	19	8		76	21	3				
96	SENTHIL	48	M	6870	11000			2.88	10600			3.57	8700			3.3	532	ACUTE PANCREATITIS	MILD
					69	24	7		75	21	4		70	21	9				

SL NO	NAME	AGE	SEX	IP NO.	DAY 0				DAY 1				DAY 2				AMYL	USG/CT FINDING	ATLANTA CLASSIFICATION
					TC/DC			NLR	TC/DC			NLR	TC/DC			NLR			
97	PRASAD	22	M	6618	13200			11.4	12600			12.57	11400			10.3	765	ACUTE PANCREATITIS WITH ARDS	SEVERE
					91	8	1		88	7	5		82	8	10				
98	SELVI	35	F	5682	7800			7.25	8700			7.00	8900			5.5	432	ACUTE PANCREATITIS	MILD
					87	12	1		84	12	4		83	15	2				
99	RAJENDRAN	43	M	4933	8700			3.30	7600			3.57	9600			2.9	254	ACUTE PANCREATITIS	MILD
					76	23	1		75	21	4		72	25	3				
100	RAJKUMAR	40	M	2693	9800			5.60	8900			5.93	7400			3.6	345	ACUTE PANCREATITIS	MILD
					84	15	1		83	14	3		76	21	3				

Neutrophil Lymphocyte Ratio

ORIGINALITY REPORT

23%	12%	16%	5%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	Tenner, Scott, and William M. Steinberg. "Acute Pancreatitis", Sleisenger and Fordtran s Gastrointestinal and Liver Disease, 2010. Publication	4%
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